(19) World Intellectual Property Organization International Bureau

ganization
AIPT
ational Bureau
OMI



. | 1886 | 1886 | 1886 | 1886 | 1886 | 1886 | 1886 | 1886 | 1886 | 1886 | 1886 | 1886 | 1886 | 1886 | 1886 | 1

(43) International Publication Date 1 April 2004 (01.04.2004)

PCT

(10) International Publication Number WO 2004/026888 A2

(51) International Patent Classification7:

C07H

(21) International Application Number:

PCT/US2003/029577

(22) International Filing Date:

19 September 2003 (19.09.2003)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 60/412,479

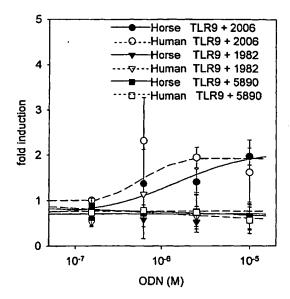
19 September 2002 (19.09.2002) US

(71) Applicants (for all designated States except US): COLEY PHARMACEUTICAL GMBH [DE/DE]; Elisabeth-Selbert-Strasse 9, 40764 Langenfeld (DE). UNIVERSITY OF SASKATCHEWAN [CA/CA]; Kirk Hall, 117 Science Place, Saskatoon, Saskatchewan S7N 5C8 (CA). QIAGEN GMBH [DE/DE]; Max-Volmer-Strasse 4, 40724 Hilden (DE).

- (72) Inventors; and
- (75) Inventors/Applicants (for US only): LIPFORD, Grayson, B. [US/US]; 38 Bates Road, Watertown, MA 02472 (US). MOOKHERJEE, Neeloffer [IN/CA]; Apt 408, 2233 Allison Road,, Vancouver, BC V6T IT7 (CA). BABIUK, Lorne [CA/CA]; 245 East Place, Saskatoon, Saskatchewan S7J 2Y1 (CA). BROWNLIE, Robert [CA/CA]; 123 O'Brien Crescent, Saskatoon, Saskatchewan S7K 5K3 (CA). GRIEBEL, Philip [CA/CA]; Box 36, RR5, Saskatoon, Saskatchewan S7K 3J8 (CA). MUTWIRI, George [CA/CA]; 569 Nordstrum Road, Saskatoon, Saskatchewan S7K 7X6 (CA). HECKER, Rolf [DE/DE]; Benrodestr. 60, 40597 Düsseldorf (DE).
- (74) Agent: STEELE, Alan, W.; Wolf, Greenfield & Sacks, P.C., 600 Atlantic Avenue, Boston, MA 02210 (US).
- (81) Designated States (national): AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX,

[Continued on next page]

(54) Title: TOLL-LIKE RECEPTOR 9 (TLR9) FROM VARIOUS MAMMALIAN SPECIES



(57) Abstract: Novel amino acid and nucleotide sequences for rat, pig (porcine), cow (bovine), horse (equine), and sheep (ovine) Toll-like receptor 9 (TLR9) are provided. Also provided are amino acid and nucleotide sequences for dog (canine), cat (feline), mouse (murine), and human TLR9. Comparison of these sequences, especially in combination with functional assessment for species-specific CpG motif preferences, permits identification of specific regions and amino acid residues of interest in TLR9 ligand interaction. Novel chimeric TLR9 receptor molecules, cells expressing these molecules, and methods for their use in screening assays for TLR9 ligands are also provided.



WO 2004/026888 A2



MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,

SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

 without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

TOLL-LIKE RECEPTOR 9 (TLR9) FROM VARIOUS MAMMALIAN SPECIES

Background of the Invention

Synthetic oligodeoxynucleotides (ODN) and DNA containing immunostimulatory CpG motifs (CpG DNA) function as potent adjuvants and activators of the innate immune system. Heeg K et al. (2000) *Int Arch Allergy Immunol* 121:87-97; Krieg AM (2001) *Vaccine* 19:618-22. A wide variety of CpG-containing sequences have been screened for biological activity and it is reported that optimal CpG DNA sequences can vary among species. Rankin R et al. (2001) *Antisense Nucleic Acid Drug Dev* 11:333-40.

Toll-like receptor 9 (TLR9) has recently been identified as a receptor for CpG ODN. Hemmi H et al. (2000) *Nature* 408:740-5. The molecular mechanism by which TLR9 recognizes CpG DNA is not understood.

10

15

20

25

30

Summary of the Invention

Toll-like receptor 9 (TLR9) is known to be involved in innate immunity and to signal in response to CpG DNA. To date, the amino acid sequences only of human and murine TLR9 have been reported, and, interestingly, these two species are known to prefer different CpG motifs. The structural basis for this species-specific CpG motif preference has not yet been fully elucidated. The instant invention provides, in part, novel amino acid and nucleotide sequences of rat, pig, cow, and horse TLR9. These novel TLR9 sequences are useful for elucidating certain key structural features of TLR9. Specifically, comparison of sequences of murine, human, and these novel TLR9 sequences permits identification of areas of highly conserved sequence, areas of group conservation, and areas of hypervariability. In addition, such comparisons permit an assessment of evolutionary relatedness among TLR9 molecules of the various species, as well as an assessment of inter-species homologies. Importantly, such comparisons permit a rational basis for identifying amino acids in TLR9 that may be involved in the CpG binding site, as well as amino acids involved in conferring species specificity for particular CpG motifs. Such information may be used to design and construct novel TLR9 molecules which incorporate specific point or regional mutations and which possess desired ligand binding characteristics. Such information may also be useful in designing and identifying novel ligands for TLR9 of a given species.

In one aspect, the invention provides isolated polypeptides having amino acid sequences for rat, pig (porcine), cow (bovine), horse (equine), and sheep (ovine) TLR9 polypeptides. These amino acid sequences correspond to SEQ ID NOs 1, 5, 9, 13, and 17, respectively. Each of these sequences is believed to include at least a majority of an extracellular domain, as well as a transmembrane region and at least part of a TLR/IL-1 receptor (TIR) domain. To the extent any such sequence may lack an amino-terminal and/or carboxy-terminal sequence, such sequence is ascertainable, without undue experimentation, using conventional molecular biology techniques and the sequence information provided herein.

5

10

15

20

25

30

In another aspect the invention provides isolated polypeptides having amino acid sequences for essentially the whole extracellular domain, optionally including a signal peptide, of each of rat, porcine, bovine, equine, and ovine TLR9. These amino acid sequences correspond to SEQ ID NOs 2, 6, 10, 14, and 18, respectively. Such extracellular domains are believed to include sequence specifically involved in binding to TLR9 ligand, such as CpG DNA. In addition, such extracellular domains are believed to include sequence that confers species specificity for particular CpG motifs.

Isolated nucleic acid molecules encoding the polypeptides just described above are also provided according to further aspects of the invention. Such nucleic acid molecules include, but are not limited to, nucleic acid molecules having sequences provided by SEQ ID NOs 3, 7, 11, 15, 19; and 4, 8, 12, 16, and 20, respectively. Isolated nucleic acid molecules encoding the TLR9 polypeptides of SEQ ID NOs 1, 5, 9, 13, 17; and 2, 6, 10, 14, and 18 also include nucleic acid molecules that differ in sequence from SEQ ID NOs 3, 7, 11, 15, 19; and 4, 8, 12, 16, and 20, respectively, due to degeneracy of the genetic code. Such nucleic acid molecules will hybridize, under stringent conditions, with suitably selected nucleic acid molecules having sequences selected from SEQ ID NOs 3, 4, 7, 8, 11, 12, 15, 16, 19, and 20.

In another aspect the invention provides a vector which includes an isolated nucleic acid molecule of the invention. In one embodiment the vector is an expression vector and the isolated nucleic acid molecule of the invention is operably linked to a regulatory sequence in the vector. When present within a cell, an expression vector according to this aspect of the invention causes the cell to express a polypeptide of the invention.

The invention according to another aspect provides a cell in which a vector of the invention is present. In one embodiment the cell containing the vector expresses a

- 3 -

polypeptide of the invention. In certain embodiments the cell also contains a reporter construct that transduces a TLR9-mediated signal in response to contact of the polypeptide of the invention or a TLR9 with a suitable TLR9 ligand. The cell containing the vector, and optionally containing the reporter construct, can be used in screening methods also provided by the invention.

5

10

15

20

25

30

In yet another aspect the invention provides an antibody or antibody fragment that binds specifically to an isolated polypeptide of the invention. In certain embodiments the antibody or antibody fragment binds uniquely to one of rat, porcine, bovine, equine, or ovine TLR9 polypeptide. More specifically, the antibody or antibody fragment binds uniquely to one of the isolated polypeptides of the invention. In one embodiment the antibody or antibody fragment that binds uniquely to one of rat, porcine, bovine, equine, or ovine TLR9 polypeptide also binds to either mouse or human TLR9. In another embodiment the antibody or antibody fragment that binds uniquely to one of rat, porcine, bovine, equine, or ovine TLR9 polypeptide does not also bind to either mouse or human TLR9. In some embodiments the antibody or antibody fragment binds selectively to a chimeric TLR9 polypeptide of the invention. In certain embodiments the antibody or antibody fragment of the invention is a monoclonal antibody or fragment of a monoclonal antibody.

In one aspect the invention provides a method for identifying key amino acids in a TLR9 of a first species which confer specificity for CpG DNA optimized for TLR9 of the first species. The method involves aligning protein sequences of TLR9 of a first species, TLR9 of a second species, and TLR9 of a third species, wherein the TLR9 of the third species preferentially generates a signal when contacted with a CpG DNA optimized for TLR9 of the first species rather than when contacted with a CpG DNA optimized for TLR9 of the second species; generating an initial set of candidate amino acids in the TLR9 of the first species by excluding each amino acid in the TLR9 of the first species which (a) is identical with the TLR9 of the second species or (b) differs from the TLR9 of the second species only by conservative amino acid substitution; generating a refined set of candidate amino acids in the TLR9 of the first species which (a) is identical with the TLR9 of the third species or (b) differs from the TLR9 of the third species only by conservative amino acids in the TLR9 of the third species only by conservative amino acid substitution; and identifying as key amino acids in the TLR9 of the first species each amino acid in the refined set of candidate amino acids.

-4-

In another aspect the invention provides a method for identifying key amino acids in human TLR9 which confer specificity for CpG DNA optimized for human TLR9. The method according to this aspect of the invention involves aligning protein sequences of human TLR9, murine TLR9, and TLR9 of a third species, wherein the TLR9 of the third species preferentially generates a signal when contacted with a CpG DNA optimized for human TLR9 rather than when contacted with a CpG DNA optimized for murine TLR9; generating an initial set of candidate amino acids in human TLR9 by excluding each amino acid in human TLR9 which (a) is identical with murine TLR9 or (b) differs from murine TLR9 only by conservative amino acid substitution; generating a refined set of candidate amino acids by selecting each amino acid in the initial set of candidate amino acids in human TLR9 which (a) is identical with the TLR9 of the third species or (b) differs from the TLR9 of the third species only by conservative amino acid substitution; and identifying as key amino acids in human TLR9 each amino acid in the refined set of candidate amino acids. In one embodiment the method according to this aspect of the invention is performed iteratively with a plurality of TLR9s derived from different species other than human and mouse, wherein for each TLR9 the refined set of candidate amino acids is assigned a weight corresponding to a ratio equal to (responsiveness to human-preferred CpG DNA)/(responsiveness to murine-preferred CpG DNA).

5

10

15

20

25

30

In another aspect the invention also provides an isolated polypeptide having an amino acid sequence identical to SEQ ID NO:30 (extracellular domain (ECD) of murine TLR9) except for substitution of at least one key amino acid identified according to the method above. The polypeptide according to this aspect of the invention is a chimeric TLR9 polypeptide. Preferably the polypeptide according to this aspect of the invention binds to CpG DNA optimized for human TLR9 better than does the isolated polypeptide having an amino acid sequence identical to SEQ ID NO:30 (ECD of murine TLR9). In one embodiment the polypeptide includes only one substituted amino acid. The isolated polypeptide according to this aspect of the invention may further include sequence involved in TLR/IL-1R signal transduction, e.g., intracellular domain of TLR9 as provided in SEQ ID NOs 29 and 33. For example, in one embodiment a polypeptide according to this aspect of the invention is an isolated polypeptide having an amino acid sequence identical to SEQ ID NO:29 (full length murine TLR9) except for substitution of at least one key amino acid identified according to the method above.

5

10

15

20

In another aspect the invention provides an isolated nucleic acid molecule including a nucleic acid sequence encoding a chimeric TLR9 polypeptide just described. In one embodiment the isolated nucleic acid molecule has a nucleic acid sequence encoding a chimeric TLR9 polypeptide just described.

In yet another aspect, the invention provides a screening method to identify a TLR9 ligand. The method involves contacting a polypeptide (including a chimeric TLR9 polypeptide) of the invention with a candidate TLR9 ligand; measuring a signal in response to the contacting; and identifying the candidate TLR9 ligand as a TLR9 ligand when the signal in response to the contacting is consistent with TLR9 signaling. In one embodiment the candidate TLR9 ligand is an immunostimulatory nucleic acid. In one embodiment the candidate TLR9 ligand is a CpG DNA.

The invention also provides, in yet a further aspect, a screening method to identify species-specific CpG-motif preference of an isolated polypeptide of the invention. The method according to this aspect of the invention involves contacting an isolated polypeptide of the invention with a CpG DNA including a hexamer sequence selected from the group consisting of GACGTT, AACGTT, CACGTT, TACGTT, GGCGTT, GCCGTT, GTCGTT, GATGTT, GAAGTT, GAGGTT, GACGTT, GA

TCCATGACGTTTTTGATGTT (SEQ ID NO:39), TCCATAACGTTTTTGATGTT (SEQ ID NO:40), TCCATCACGTTTTTGATGTT (SEQ ID NO:41), TCCATTACGTTTTTGATGTT (SEQ ID NO:42), 25 TCCATGGCGTTTTTGATGTT (SEQ ID NO:43), TCCATGCCGTTTTTGATGTT (SEQ ID NO:44), TCCATGTCGTTTTTTGATGTT (SEQ ID NO:45), TCCATGATGTTTTTGATGTT (SEQ ID NO:46), TCCATGAAGTTTTTGATGTT (SEQ ID NO:47), 30 TCCATGAGGTTTTTGATGTT (SEQ ID NO:48), TCCATGACATTTTTGATGTT (SEQ ID NO:49), TCCATGACCTTTTTGATGTT (SEQ ID NO:50), (SEQ ID NO:51), TCCATGACTTTTTTGATGTT TCCATGACGCTTTTGATGTT (SEQ ID NO:52), 35 TCCATGACGATTTTGATGTT (SEQ ID NO:53), TCCATGACGGTTTTGATGTT (SEQ ID NO:54),

- 6 -

TCCATGACGTCTTTGATGTT (SEQ ID NO:55), TCCATGACGTATTTGATGTT (SEQ ID NO:56), and TCCATGACGTGTTTGATGTT (SEQ ID NO:57).

In certain embodiments of the screening methods of the invention, the signal includes expression of a reporter gene responsive to TLR/IL-1R signal transduction pathway. In one embodiment the reporter gene is operatively linked to a promoter sensitive to NF-kB. In one embodiment the signal in response to contacting is binding of the candidate TLR9 ligand or CpG DNA to the polypeptide of the invention.

In one embodiment the screening method is performed on a plurality of test compounds. In one embodiment the response mediated by the TLR9 signal transduction pathway is measured quantitatively and the response mediated by the TLR9 signal transduction pathway associated with each of the plurality of test compounds is compared with a response arising as a result of an interaction between the functional TLR9 and a reference immunostimulatory compound.

15

20

25

30

10

Brief Description of the Figures

Figure 1 depicts a Clustal W multiple sequence alignment of deduced amino acid sequences for cat (feline), dog (canine), cow (bovine), mouse (murine), sheep (ovine), pig (porcine), horse (equine), human, and rat TLR9 polypeptides. The deduced amino acid sequences for feline, canine, bovine, murine, ovine, porcine, equine, human, and rat TLR9 polypeptides shown in the figure correspond to SEQ ID NOs 25, 21, 9, 29, 17, 5, 13, 33, and 1, respectively. Lines labeled "multiple" refer to the multiple sequence alignment of all six sequences shown. Lines labeled "mo/hu" refer to a paired sequence alignment of mouse and human TLR9 sequences alone.

Figure 2 is a cladogram depicting an evolutionary relatedness tree for rat, murine, porcine, bovine, equine, and human TLR9 polypeptides in Figure 1.

Figure 3 is a graph depicting species specificity of TLR9 signaling with selected oligonucleotides having strong specificity for human (2006), mouse (5890), or neither (1982).

Detailed Description of the Invention

The present invention provides novel amino acid and nucleotide sequences for TLR9 derived from rat, pig, cow, horse, and sheep. These sequences can be used to identify key features of the primary sequences of these and related TLR molecules, including previously

10

15

20

25

30

known primary sequences of human and mouse (murine) TLR9. Such key features include binding site information and species specificity toward particular CpG motifs. Native and novel chimeric TLR9 polypeptides designed with the aid of this information can be expressed in vitro or in vivo and used in screening assays to identify and to design novel TLR9 ligands. Additionally, the native and novel chimeric TLR9 polypeptides designed with the aid of this information can be expressed in vitro or in vivo and used in screening assays to compare various TLR9 ligands, including CpG DNA.

In one aspect the invention provides isolated TLR9 polypeptides, and isolated nucleic acid molecules encoding them, from rat, pig, cow, horse, and sheep. The term "isolated" as used herein with reference to a nucleic acid molecule or polypeptide means substantially free of or separated from components with which it is normally associated in nature, e.g., other nucleic acids, proteins, lipids, carbohydrates or *in vivo* systems to an extent practical and appropriate for its intended use. In particular, the nucleic acids or polypeptides are sufficiently pure and are sufficiently free from other biological constituents of host cells so as to be useful in, for example, producing pharmaceutical preparations. Because an isolated nucleic acid or polypeptide of the invention may be admixed with a pharmaceutically acceptable carrier in a pharmaceutical preparation, the nucleic acid or polypeptide may represent only a small percentage by weight of such a preparation. The nucleic acid or polypeptide is nonetheless substantially pure in that it has been substantially separated from the substances with which it may be associated in living systems.

An amino acid sequence of rat TLR9 is provided as SEQ ID NO:1. Based on comparison with known amino acid sequences of human and murine TLR9, it appears that SEQ ID NO:1 includes sequence for at least a majority of the extracellular domain, all of the transmembrane domain, and at least a portion of the intracellular domain of rat TLR9 (See Figure 1). Amino acids numbered 1-821 of SEQ ID NO:1 are presumptively extracellular domain and correspond to SEQ ID NO:2. SEQ ID NO:3 is a nucleotide sequence of rat TLR9 cDNA having an open reading frame corresponding to nucleotides 1-3096. SEQ ID NO:4 is a nucleotide sequence of rat cDNA encoding amino acids 1-821 of SEQ ID NO:1.

An amino acid sequence of porcine TLR9 is provided as SEQ ID NO:5. Based on comparison with known amino acid sequences of human and murine TLR9, it appears that SEQ ID NO:5 includes sequence for at least a majority of the extracellular domain, all of the transmembrane domain, and at least a portion of the intracellular domain of porcine TLR9

-8-

(See Figure 1). Amino acids numbered 1-819 of SEQ ID NO:5 are presumptively extracellular domain and correspond to SEQ ID NO:6. SEQ ID NO:7 is a nucleotide sequence of porcine TLR9 cDNA having an open reading frame corresponding to nucleotides 77-3166. SEQ ID NO:8 is a nucleotide sequence of porcine cDNA encoding amino acids 1-819 of SEQ ID NO:5.

5

10

15

20

25

30

An amino acid sequence of bovine TLR9 is provided as SEQ ID NO:9. Based on comparison with known amino acid sequences of human and murine TLR9, it appears that SEQ ID NO:9 includes sequence for at least a majority of the extracellular domain, all of the transmembrane domain, and at least a portion of the intracellular domain of bovine TLR9 (See Figure 1). Amino acids numbered 1-818 of SEQ ID NO:9 are presumptively extracellular domain and correspond to SEQ ID NO:10. SEQ ID NO:11 is a nucleotide sequence of bovine TLR9 cDNA having an open reading frame corresponding to nucleotides 84-3170. SEQ ID NO:12 is a nucleotide sequence of bovine cDNA encoding amino acids 1-818 of SEQ ID NO:9.

An amino acid sequence of equine TLR9 is provided as SEQ ID NO:13. Based on comparison with known amino acid sequences of human and murine TLR9, it appears that SEQ ID NO:13 includes sequence for at least a majority of the extracellular domain, all of the transmembrane domain, and at least a portion of the intracellular domain of equine TLR9 (See Figure 1). Amino acids numbered 1-820 of SEQ ID NO:13 are presumptively extracellular domain and correspond to SEQ ID NO:14. SEQ ID NO:15 is a nucleotide sequence of equine TLR9 cDNA having an open reading frame corresponding to nucleotides 115-3207. SEQ ID NO:16 is a nucleotide sequence of equine cDNA encoding amino acids 1-820 of SEQ ID NO:13.

An amino acid sequence of ovine TLR9 is provided as SEQ ID NO:17. Based on comparison with known amino acid sequences of human and murine TLR9, it appears that SEQ ID NO:17 includes sequence for at least a majority of the extracellular domain, all of the transmembrane domain, and at least a portion of the intracellular domain of ovine TLR9 (See Figure 1). Amino acids numbered 1-818 of SEQ ID NO:17 are presumptively extracellular domain and correspond to SEQ ID NO:18. SEQ ID NO:19 is a nucleotide sequence of ovine TLR9 cDNA having an open reading frame corresponding to nucleotides 92-3178. SEQ ID NO:20 is a nucleotide sequence of ovine cDNA encoding amino acids 1-818 of SEQ ID NO:17.

PCT/US2003/029577

SEQ ID NO:1 (Rat TLR9)

MVLCRRTLHPLSLLVOAAVLAEALALGTLPAFLPCELKPHGLVDCNWLFLKSVPHFSAAEPRSNITSLSLIANRI HHLHNLDFVHLPNVRQLNLKWNCPPPGLSPLHFSCRMTIEPKTFLAMRMLEELNLSYNGITTVPRLPSSLTNLSL SHTNILVLDASSLAGLHSLRVLFMDGNCYYKNPCNGAVNVTPDAFLGLSNLTHLSLKYNNLTEVPRQLPPSLEYL 5 $\verb|LLSYNLIVKLGAEDLANLTSLRMLDVGGNCRRCDHAPDLCTECRQKSLDLHPQTFHHLSHLEGLVLKDSSLHSLN|$ SKWFQGLANLSVLDLSENFLYESINKTSAFQNLTRLRKLDLSFNYCKKVSFARLHLASSFKSLVSLQELNMNGIF FRLLNKNTLRWLAGLPKLHTLHLQMNFINQAQLSVFSTFRALRFVDLSNNRISGPPTLSRVAPEKADEAEKGVPW PASLTPALPSTPVSKNFMVRCKNLRFTMDLSRNNQVTIKPEMFVNLSHLQCLSLSHNCIAQAVNGSQFLPLTNLK VLDLSYNKLDLYHSKSFSELPQLQALDLSYNSQPFSMQGIGHNFSFLANLSRLQNLSLAHNDIHSRVSSRLYSTS 10 VEYLDFSGNGVGRMWDEEDLYLYFFODLRSLIHLDLSONKLHILRPONLNYLPKSLTKLSFRDNHLSFFNWSSLA FLPNLRDLDLAGNLLKALTNGTLPNGTLLOKLDVSSNSIVFVVPAFFALAVELKEVNLSHNILKTVDRSWFGPIV MNLTVLDVSSNPLHCACGAPFVDLLLEVQTKVPGLANGVKCGSPRQLQGRSIFAQDLRLCLDDVLSRDCFGLSLL AVAVGTVLPLLOHLCGWDVWYCFHLCLAWLPLLTRGRRSAQALPYDAFVVFDKAQSAVADWVYNELRVRLEERRG RRALRLCLEDRDWLPGQTLFENLWAS I YGSRKTLFVLAHTDKVSGLLRTSFLLAQQRLLEDRKDVVVLV I LRPDA HRSRYVRLRQRLCRQSVLFWPHQPNGQGSFWAQLSTALTRDNHHFYNRNFCRGPTAE

SEQ ID NO:2 (Rat TLR9)

MVLCRRTLHPLSLLVQAAVLAEALALGTLPAFLPCELKPHGLVDCNWLFLKSVPHFSAAEPRSNITSLSLIANRI
HHLHNLDFVHLPNVRQLNLKWNCPPPGLSPLHFSCRMTIEPKTFLAMRMLEELNLSYNGITTVPRLPSSLTNLSL
SHTNILVLDASSLAGLHSLRVLFMDGNCYYKNPCNGAVNVTPDAFLGLSNLTHLSLKYNNLTEVPRQLPPSLEYL
LLSYNLIVKLGAEDLANLTSLRMLDVGGNCRRCDHAPDLCTECRQKSLDLHPQTFHHLSHLEGLVLKDSSLHSLN
SKWFQGLANLSVLDLSENFLYESINKTSAFQNLTRLRKLDLSFNYCKKVSFARLHLASSFKSLVSLQELNMNGIF
FRLLNKNTLRWLAGLPKLHTLHLQMNFINQAQLSVFSTFRALRFVDLSNNRISGPPTLSRVAPEKADEAEKGVPW
25 PASLTPALPSTPVSKNFMVRCKNLRFTMDLSRNNQVTIKPEMFVNLSHLQCLSLSHNCIAQAVNGSQFLPLTNLK
VLDLSYNKLDLYHSKSFSELPQLQALDLSYNSQPFSMQGIGHNFSFLANLSRLQNLSLAHNDIHSRVSSRLYSTS
VEYLDFSGNGVGRMWDEEDLYLYFFQDLRSLIHLDLSQNKLHILRPQNLNYLPKSLTKLSFRDNHLSFFNWSSLA
FLPNLRDLDLAGNLLKALTNGTLPNGTLLQKLDVSSNSIVFVVPAFFALAVELKEVNLSHNILKTVDRSWFGPIV
MNLTVLDVSSNPLHCACGAPFVDLLLEVQTKVPGLANGVKCGSPRQLQGRSIFAQDLRLCLDDVLSRDCFG

SEQ ID NO:3 (Rat TLR9)

30

40

45

50

atqqttctctqtcqcaqqaccctqcaccccttqtctctctggtacagqccgcaqtgctggctgaggctctggcc ctgggtaccctgcctgccttcctaccctgtgaactgaagcctcatggcctggtagactgcaactggctcttcctg aagtetgtgceteacttetetgecgcagaaccccgttecaacateaccagcettteettgategccaaccgcate caccacctgcacaacctcgactttgtccacctgcccaacgtgcgacagctgaacctcaagtggaactgtccgccc cctqqcctcaqcccttqcacttctcctqcqcatqaccattqaqccaaaaccttcctqqctatqcqcatqctq qaaqaqctgaacctqaqctataacqqtatcaccactqtgccccqcctgcccaqctccctgacqaatctgaqccta agccacaccaacatcctqqtactcqatqccaqcaqcctcqctqqcctqcacaqcctqcqaqttctcttcatqqac qqqaactqctactacaaqaacccctqcaacqqqqqqqtqaacqtqaccccqqacqccttcctqqqcttgaqcaac ctcacccacttgtcccttaagtataacaacctcacagaggtgccccgccaactgccccccagcctggagtacctc ctgctgtcctataacctcatcgtcaagctgggggccgaagacctagccaacctgacctcccttcgaatgcttgat gtgggtgggaattgccgtcgctgtgatcacgcccccgacctctgtacagaatgccggcagaagtcccttgatctg caccctcagactttccatcacctgagccaccttgaaggcctggtgctgaaggacagttctctccactcgctgaac tecaaqtgqttecaqqqtetqqegaaceteteggtgetggacetaagegagaaetttetetacqagageateaae aaaaccaqcqcctttcaqaacctgacccgtctgcgcaagctcgacctgtccttcaattactgcaagaaggtatcg ttcgcccgcctccacctggcaagttccttcaagagcctggtgtcgctgcaggagctgaacatgaacggcatcttc aatttcatcaaccaggcgcagctcagcgtctttagtaccttccgagcccttcgcttttgtggacctgtccaataat cqcatcagegggcetecaacgetgtecagagtegcececgaaaaggcagacgaggeggagaaggggttecatgg cctgcaagtctcaccccagctctcccgagcactcccgtctcaaagaacttcatggtcaggtgtaagaacctcaga ttcaccatggacctgtctcggaacaaccaggtgactatcaagccagagatgttcgtcaacctctcccatctccag tgtctgagcctgagccacaactgcatcgcgcaggctgtcaatggctctcagttcctgccgctgaccaacctgaag gtgctggacctgtcctataacaagctggacctgtaccattcgaaatcgttcagtgagctcccacagttgcaggcc

ctggacctgagctacaacagccagccattcagcatgcaggggataggccacaacttcagttttctggccaatctg tccaggttacagaaccttagcctggcacacaatgacattcacagccgcgtgtcctcacgcctctacagcacctca gtggagtatctggacttcagcggcaacggtgtgggccgcatgtgggacgaggaggacctttacctctatttcttc caagacctgagaagcctgattcatctggacctgtctcagaataagctgcacatcctccggcccagaacctcaac 5 ttcctgcccaatctgcgagacctggacctggcaggcaatctactaaaggccctgaccaacggcaccctgcctaat ggcacgetectecagaaactggatgtcagtagcaacagtategtetttgtggteceageettetttgetetggeg gtagagetaaaagaggteaaceteageeataacateeteaagaetgtggategeteetggtttgggeeeattgtg atgaacctgacggttctagacgtgagcagcaaccctctgcattgtgcctgcggtgcaccctttgtagacttactg 10 ctggaagtgcagaccaaggtgcctggcctggctaacggtgtgaagtgtggcagtccccgccagctgcagggccgc agcatctttgcgcaagacctgcggctgtgcctggatgacgtcctttctcgggactgcttttggcctttcactcctg gctgtggccgtgggcacggtgttgcctttactgcagcatctctgcggctgggacgtctggtactgtttccatctg tgcctggcatggctacctttgctgacccgtggccggcgcagcgcccaagctctcccttatgatgccttcgtggtg ttcgataaggcgcagagcgcggttgctgactgggtgtataacgagcttcgagtgcggctagaggagcgcgcggt 15 cgccgagccctacgcttgtgtctggaggaccgagattggctgcctggccagacactcttcgagaacctctgggcc tccatctatggcagccgcaagactctgtttgtgctggcccacacggacaaggtcagtggcctcctgcgcaccagc $\verb|caceg| ctcccgctacgtgcgactgcgcctctgccgccagagtgtgctcttctggccccatcagcccaac| \\$ gggcagggcagcttctgggcccagctgagtacagccctgactagggacaaccacctctataaccggaacttc 20 tgccggggacctacagcagaatag

SEQ ID NO:4 (Rat TLR9)

atggttetetgtegeaggaccetgcacceettgteteteetggtacaggeegeagtgetgggetgaggetetggee ctgggtaccctgccttcctaccctgtgaactgaagcctcatggcctggtagactgcaactggctcttcctg 25 aagtotgtgcotcacttototgcogcagaaccccgttocaacatcaccagcotttoottgatogccaaccgcato caccacctgcacacctcgactttgtccacctgcccaacgtgcgacagctgaacctcaagtggaactgtccgccc cctggcctcagccccttgcacttctcctgccgcatgaccattgagcccaaaaccttcctggctatgcgcatgctg gaagagctgaacctgagctataacggtatcaccactgtgccccgcctgcccagctccctgacgaatctgagccta agccacaccaacatcctggtactcgatgccagcagcctcgctggcctgcacagcctgcgagttctcttcatggac 30 gggaactgctactacaagaacccctgcaacgggggggtgaacgtgaccccggacgccttcctgggcttgagcaac ctcacccacttgtcccttaagtataacaacctcacagaggtgccccgccaactgccccccagcctggagtacctc ctgctgtcctataacctcatcgtcaagctgggggccgaagacctagccaacctgacctcccttcgaatgcttgat gtgggtgggaattgccgtcgctgtgatcacgcccccgacctctgtacagaatgccggcagaagtcccttgatctg caccctcagactttccatcacctgagccaccttgaaggcctggtgctgaaggacagttctctccactcgctgaac 35 ${\tt tccaagtggttccagggtctggcgaacctctcggtgctggacctaagcgagaaccttctctacgagagcatcaac}$ aaaaccagcgcctttcagaacctgacccgtctgcgcaagctcgacctgtccttcaattactgcaagaaggtatcg $\verb|ttegccegectccacetggcaagtteettcaagagcetggtgtegetgcaggagctgaacatgaacggcatette|$ aatttcatcaaccaggcgcagctcagcgtctttagtaccttccgagcccttcgctttgtggacctgtccaataat 40 cgcatcagcgggcctccaacgctgtccagagtcgcccccgaaaaggcagacgagggggagaagggggttccatgg cctqcaaqtctcacccagctctcccgaqcactcccqtctcaaagaacttcatggtcaggtgtaagaacctcaga ttcaccatggacctgtctcggaacaaccaggtgactatcaagccagagatgttcgtcaacctctcccatctccag tgtctgagcctgagccacaactgcatcgcgcaggctgtcaatggctctcagttcctgccgctgaccaacctgaag gtgctggacctgtcctataacaagctggacctgtaccattcgaaatcgttcagtgagctcccacagttgcaggcc 45 ctggacctgagctacaacagccagccattcagcatgcaggggataggccacaacttcagttttctggccaatctg tccaggttacagaaccttagcctggcacacaatgacattcacagccgcgtgtcctcacgcctctacagcacctca gtggagtatetggaetteageggcaaeggtgtgggeegeatgtgggaegaggaggaeetttaeetetatteete caagacctgagaagcctgattcatctggacctgtctcagaataagctgcacatcctccggccccagaacctcaac 50 $\verb|tcctgcccaatctgcgagacctggacctggcaggcaatctactaaaaggccctgaccaaccggcaccctgcctaat|$ ggcacgctcctccagaaactggatgtcagtagcaacagtatcgtctttgtggtcccagccttctttgctctggcg gtagagctaaaagaggtcaacctcagccataacatcctcaagactgtggatcgctcctggtttgggcccattgtg atgaacctgacggttctagacgtgagcagcaaccctctgcattgtgcctgcggtgcaccctttgtagacttactg ctggaagtgcagaccaaggtgcctggcctagcgtaacggtgtgaagtgtggcagtccccgccagctgcagggccgc 55 agcatctttgcgcaagacctgcggctgtgcctggatgacgtcctttctcgggactgcttttggc

£ .

٠.

41, 1915 | 18₁

· The first of

" /\$". 'Ī

SEQ ID NO:5 (Porcine TLR9)

MGPRCTLHPLSLLVQVTALAAALAQGRLPAFLPCELQPHGLVNCNWLFLKSVPHFSAAAPRANVTSLSLLSNRIH ${\tt HLHDSDFVHLSSLRTLNLKWNCPPAGLSPMHFPCHMTIEPNTFLAVPTLEELNLSYNSITTVPALPDSLVSLSLS}$ ${\tt RTNILVLDPTHLTGLHALRYLYMDGNCYYKNPCQGALEVVPGALLGLGNLTHLSLKYNNLTEVPRSLPPSLETLL}$ ${\tt LSYNHIVTLTPEDLANLTALRVLDVGGNCRRCDHARNPCRECPKDHPKLHSDTFSHLSRLEGLVLKDSSLYNLDT}$ RWFRGLDRLQVLDLSENFLYDCITKTTAFQGLARLRSLNLSFNYHKKVSFAHLHLAPSFGHLRSLKELDMHGIFF RSLSETTLOPLVQLPMLQTLRLQMNFINQAQLSIFGAFPGLLYVDLSDNRISGAARPVAITREVDGRERVWLPSR NLAPRPLDTLRSEDFMPNCKAFSFTLDLSRNNLVTIQSEMFARLSRLECLRLSHNSISQAVNGSQFVPLTSLRVL DLSHNKLDLYHGRSFTBLPRLEALDLSYNSQPFTMQGVGHNLSFVAQLPALRYLSLAHNDIHSRVSQQLCSASLC 10 ALDFSGNDLSRMWAEGDLYLRFFOGLRSLVWLDLSONHLHTLLPRALDNLPKSLKHLHLRDNNLAFFNWSSLTLL PKLETLDLAGNOLKALSNGSLPSGTOLRRLDLSGNS IGFVNPGFFALAKOLEELNLSANALKTVEPSWFGSMVGN LKVLDVSANPLHCACGATFVGFLLEVQAAVPGLPSRVKCGSPGOLOGHSIFAODLRLCLDETLSWNCFGISLLAM ALGLVVPMLHHLCGWDLWYCFHLCLAWLPHRGQRRGADALFYDAFVVFDKAQSAVADWVYNELRVQLEERRGRRA LRLCLEERDWLPGKTLFENLWASVYSSRKTLFVLAHTDRVSGLLRASFLLAQQRLLEDRKDVVVLVILRPDAYRS 15 RYVRLRQRLCRQSVLLWPHQPRGQGSFWAQLGTALTRDNHHFYNRNFCRGPTTAE

SEQ ID NO:6 (Porcine TLR9)

MGPRCTLHPLSLLVQVTALAAALAQGRLPAFLPCELQPHGLVNCNWLFLKSVPHFSAAAPRANVTSLSLLSNRIH
HLHDSDFVHLSSLRTLNLKWNCPPAGLSPMHFPCHMTIEPNTFLAVPTLEELNLSYNSITTVPALPDSLVSLSLS
RTNILVLDPTHLTGLHALRYLYMDGNCYYKNPCQGALEVVPGALLGLGNLTHLSLKYNNLTEVPRSLPPSLETLL
LSYNHIVTLTPEDLANLTALRVLDVGGNCRRCDHARNPCRECPKDHPKLHSDTFSHLSRLEGLVLKDSSLYNLDT
RWFRGLDRLQVLDLSENFLYDCITKTTAFQGLARLRSLNLSFNYHKKVSFAHLHLAPSFGHLRSLKELDMHGIFF
RSLSETTLQPLVQLPMLQTLRLQMNFINQAQLSIFGAFPGLLYVDLSDNRISGAARPVAITREVDGRERVWLPSR
NLAPRPLDTLRSEDFMPNCKAFSFTLDLSRNNLVTIQSEMFARLSRLECLRLSHNSISQAVNGSQFVPLTSLRVL
DLSHNKLDLYHGRSFTELPRLEALDLSYNSQPFTMQGVGHNLSFVAQLPALRYLSLAHNDIHSRVSQQLCSASLC
ALDFSGNDLSRMWAEGDLYLRFFQGLRSLVWLDLSQNHLHTLLPRALDNLPKSLKHLHLRDNNLAFFNWSSLTLL
PKLETLDLAGNQLKALSNGSLPSGTQLRRLDLSGNSIGFVNPGFFALAKQLEELNLSANALKTVEPSWFGSMVGN
LKVLDVSANPLHCACGATFVGFLLEVQAAVPGLPSRVKCGSPGOLOGHSIFAODLRCLDETLSWNCFG

30 SEQ ID NO:7 (Porcine TLR9)

35

40

50

 ${\tt gggcaggctgcctgccttcctgccctgtgagctccagccccacggcctggtgaactgcaactggctcttcctgaa}$ gtccgtgccccacttctcggcggcagcgccccgggccaacgtcaccagcctctccttactctccaaccgcatcca ccacctgcacgactccgacttcgtccacctgtccagcctacgaactctcaacctcaagtggaactgcccgccggc tggcctcagccccatgcacttcccctgccacatgaccatcgagcccaacaccttcctqqccqtqcccaccctqqa caactgctactacaagaacccctgccagggggcgctggaggtggtgccgggtgccctcctcggcctgggcaacct cacacatctctcactcaagtacaacaatctcacggaggtgccccgcagcctgccccccagcctggagaccctgct ${\tt gttgtcctacaaccacattgtcaccctgacgcctgaggacctggccaatctgactgccctgcgcgtgcttgatgt}$ gggggggaactgccgccgctgtgaccatgcccgcaacccctgcagggagtgcccaaaggaccaccccaagctgca ctctgacaccttcagccacctgagccgcctcgaaggcctggtgttgaaagacagttctctctacaacctggacac gaccaeggccttccagggcctggcccgactgcgcagcctcaacctgtccttcaattaccacaagaaggtgtcctt ccgctcgctcagtgagaccacgctccaacctctqqtccaactgcctatqctccaqaccctqcqcctqcaqatqaa cttcattaaccaggcccagctcagcatctttqqqqccttccctqqcctqctqtacqtqqacctatcqqacaaccq catcagcggagctgcaaggccagtggccattactagggaggtggatggtagggagagggtctggcttgccttccag gaacctcgctccacgtccactggacactctccgctcagaggacttcatgccaaactgcaaggccttcagcttcac $\verb|cttggacctgtctcggaacaacctggtgacaatccagtcggagatgtttgctcgcctctcacgcctcgagtgcct|\\$ $\verb|gcgcctgagccacaacagcatctcccaggcggtcaatggctctcagtttgtgccgctgaccagcctgcgggtgct|$ ggacctgtcccacaacaagctggacctgtatcacgggcqctcqttcacqgagctgccqcgcctqqaaqcactgga cctcagctacaatagccagccctttaccatgcagggtgtggqccacaacctcagcttcgtggcccagctqcccgc

cctgcgctacctcagcctggcgcacaatgacatccatagccgagtgtcccagcagctctgtagcgcctcactgtg egecetggaetttageggeaaegatetgageeggatgtgggetgagggagaeetetateteegettetteeaagg $\verb|cctaagaagcctagtctggacctgtcccagaaccacctgcacaccctcctgccacgtgccctggacaacct|\\$ $\verb|cccc| a a a g c c t g a a g c a t c t c c g t g a c a a t a a c c t g g c c t c t t c t a a c t g g a g c c t g a c c t c c t$ gcccaagctggaaaccctggacttggctggaaaccagctgaaggccctaagcaatggcagcctgccatctggcac $\verb|ccagctgcggaggctggacctcagtggcaacagcatcggctttgtgaaccctggcttctttgccctggccaagca|\\$ gttagaagageteaaceteagegeeaatgeeeteaagaeagtggageeeteetggtttggetegatggtgggeaa cctgaaagtcctagacgtgagcgccaaccctctgcactgtgcctgtggggcgaccttcgtgggcttcctgctgca ggtacaggctgccgtgcctgggctgcccagccgcgtcaagtgtggcagtccggggcagctccagggccatagcat 10 ctttgcgcaagacctgcgcctctgcctggatgagaccctctcgtggaactgttttggcatctcgctgctggccat ggccctgggcctggttgtgcccatgctgcaccacctctgcggctgggacctctggtactgcttccacctgtgcct ggcctggctgcccaccgagggcagcggggggcgcagacgccctgttctatgatgccttcgtggtctttgacaa ageteagagtgetgtggeegaetgggtgtaeaaegagetgegggtgeagetggaggagegeegtgggegeegege actgcgcctgtgcctggaggagcgagactggttacctggcaagacgctcttcgagaacctgtgggcctcagtcta 15 $\verb|cagcagccgcaagaccetg| ttgtgctggeccacacggaccgtgtcagcggcctcttgcgtgccagtttcctgct|$ ggcccagcagcgcctgctggaggaccgcaaggacgttgtagtgctggtgatcctgcgccccgatgcctaccgctc ccgctacgtgcggctgcgccagcgcctctgccgccagagtgtcctcctctggccccaccagccccgtgggcaggg cagcttctgggcccagctgggcacagccctgaccagggacaaccaccttctataaccggaacttctgccgggg ccccacgacagccgaatagcactgagtgacagcccagttgccccagccccctggatttgcctcttgcctgggg 20 tgccccaacctgctttgctcagccacaccactgctctgctccctgttccccaccccacccccagcctggcatgt

SEQ ID NO:8 (Porcine TLR9)

ggcaggctgcctgccttcctgccctgtgagctccagccccacggcctggtgaactgcaactggctcttcctgaag tecgtgecccaetteteggeggeagegeeeegggeeaacgteaccageeteteettaetetecaaeegeatecae cacctgcacgactccgacttcgtccacctgtccagcctacgaactctcaacctcaagtggaactgcccgccggct ggcctcagccccatgcacttcccctgccacatgaccatcgagcccaacaccttcctggccgtgcccaccctggag 30 ${\tt aactgctactacaagaacccctgccagggggcgctggaggtggtgccgggtgccctcctcggcctgggcaacctc}$ acacateteteacteaagtacaacaateteacggaggtgeceegcageetgeceeccageetggagaceetgetg ttgtcctacaaccacattgtcaccctgacgcctgaggacctggccaatctgactgccctgcgcgtgcttgatgtg ggggggaactgccgccgtgtgaccatgcccgcaacccctgcagggagtgcccaaaggaccaccccaagctgcac ${\tt tctgacaccttcagccacctgaagccgcctcgaaggcctggtgttgaaagacagttctctctacaacctggacacc}$ accaeggeetteeaggeetggeeegaetgegeageeteaacetgteetteaattaeeacaagaaggtgteettt cgctcgctcagtgagaccacgctccaacctctggtccaactgcctatgctccagaccctgcgcctgcagatgaac 40 ttcattaaccaggcccagctcagcatctttggggccttccctggcctgctgtacgtggacctatcggacaaccgc atcagcggagctgcaaggccagtggccattactagggaggtggatggtagggagagggtctggctgccttccagg aacctcgctccacgtccactggacactctccgctcagaggacttcatgccaaactgcaaggccttcagcttcacc ttggacctgtctcggaacaacctggtgacaatccagtcggagatgtttgctcgcctctcacgcctcgagtgcctg $\verb|cgcctgagccacaacagcatctcccaggcggtcaatggctctcagtttgtgccgctgaccagcctgcgggtgctg|$ gacctgtcccacaacaagctggacctgtatcacggggcgctcgttcacggagctgccgcgcctggaagcactggac ctcagctacaatagccagccctttaccatgcagggtgtgggccacaacctcagcttcgtggcccagctgcccgcc ctgcgctacctcagcctggcgcacaatgacatccatagccgagtgtcccagcagctctgtagcgcctcactgtgc gccctggactttagcggcaacgatctgagccggatgtggggctgagggagacctctatctccgcttcttccaaggc ctaaqaaqcctaqtctqqctggacctgtcccaqaaccacctqcacaccctcctqccacqtqcctqqacaacctc 50 cccaaaagcctgaagcatctgcatctccgtgacaataacctggccttcttcaactggagcagcctgaccctcctg cccaagctggaaaccctggacttggctggaaaccagctgaaggccctaagcaatggcagcctgccatctggcacc cagctgcggaggctggacctcagtggcaacagcatcggctttgtgaaccctggcttctttgccctggccaagcag ttagaagageteaaceteagegeeaatgeeeteaagacagtggageeeteetggtttggetegatggtgggeaac ctgaaagtcctagacgtgagcgccaaccctctgcactgtgcctgtggggcgaccttcgtggggcttcctgctggag 55 gtacaggctgccgtgcctgggctgcccagccgcgtcaagtgtggcagtccggggcagctccagggccatagcatc tttgcgcaagacctgcgcctctgcctggatgagaccctctcgtggaactgttttggc

- 1

- Mai

70 A 245

1900 A

- 1.00 · 1.00

SEQ ID NO:9 (Bovine TLR9)

MGPYCAPHPLSLLVQAAALAAALAEGTLPAFLPCELOPHGOVDCNWLFLKSVPHFSAGAPRANVTSLSLISNRIH HLHDSDFVHLSNLRVLNLKWNCPPAGLSPMHFPCRMTIEPNTFLAVPTLEELNLSYNGITTVPALPSSLVSLSLS HTSILVLGPTHFTGLHALRFLYMDGNCYYMNPCPRALEVAPGALLGLGNLTHLSLKYNNLTEVPRRLPPSLDTLL LSYNHIVTLAPEDLANLTALRVLDVGGNCRRCDHARNPCRECPKNFPKLHPDTFSHLSRLEGLVLKDSSLYKLEK ${\tt DWFRGLGRLQVLDLSENFLYDYITKTTIFNDLTQLRRLNLSFNYHKKVSFAHLHLASSFGSLVSLEKLDMHGIFF}$ ${\tt RSLTNITLQSLTRLPKLQSLHLQLNFINQAQLSIFGAPPSLLFVDLSDNRISGAATPAAALGEVDSRVEVWRLPR}$ ${\tt GLAPGPLDAVSSKDFMPSCNLNFTLDLSRNNLVTIQQEMFTRLSRLQCLRLSHNSISQAVNGSQFVPLTSLRVLD}$ 10 LSHNKLDLYHGRSFTELPQLEALDLSYNSQPFSMQGVGHNLSFVAQLPSLRYLSLAHNGIHSRVSOKLSSASLRA LDFSGNSLSQMWAEGDLYLCFFKGLRNLVQLDLSENHLHTLLPRHLDNLPKSLRQLRLRDNNLAFFNWSSLTVLP ${\tt RLEALDLAGNQLKALSNGSLPPGIRLQKLDVSSNSIGFVIPGFFVRATRLIBLNLSANALKTVDPSWFGSLAGTL}$ KILDVSANPLHCACGAAFVDFLLERQEAVPGLSRRVTCGSPGQLQGRSIFTQDLRLCLDETLSLDCFGLSLLMVA LGLAVPMLHHLCGWDLWYCFHLCLAHLPRRRRQRGEDTLLYDAVVVFDKVQSAVADWVYNELRVQLEERRGRRAL ${\tt RLCLEERDWLPGKTLFENLWASVYSSRKTMFVLDHTDRVSGLLRASFLLAQQRLLEDRKDVVVLVILRPAAYRSR}$ 15 YVRLRQRLCRQSVLLWPHQPSGQGSFWANLGIALTRDNRHFYNRNFCRGPTTAE

SEQ ID NO:10 (Bovine TLR9)

MGPYCAPHPLSLLVQAAALAAALAEGTLPAFLPCELQPHGQVDCNWLFLKSVPHFSAGAPRANVTSLSLISNRIH

20 HLHDSDFVHLSNLRVLNLKWNCPPAGLSPMHFPCRMTIEPNTFLAVPTLEELNLSYNGITTVPALPSSLVSLSLS
HTSILVLGPTHFTGLHALRFLYMDGNCYYMNPCPRALEVAPGALLGLGNLTHLSLKYNNLTEVPRRLPPSLDTLL
LSYNHIVTLAPEDLANLTALRVLDVGGNCRRCDHARNPCRECPKNFPKLHPDTFSHLSRLEGLVLKDSSLYKLEK
DWFRGLGRLQVLDLSENFLYDYITKTTIFNDLTQLRRLNLSFNYHKKVSFAHLHLASSFGSLVSLEKLDMHGIFF
RSLTNITLQSLTRLPKLQSLHLQLNFINQAQLSIFGAFPSLLFVDLSDNRISGAATPAAALGEVDSRVEVWRLPR

25 GLAPGPLDAVSSKDFMPSCNLNFTLDLSRNNLVTIQQEMFTRLSRLQCLRLSHNSISQAVNGSQFVPLTSLRVLD
LSHNKLDLYHGRSFTELPQLEALDLSYNSQPFSMQGVGHNLSFVAQLPSLRYLSLAHNGIHSRVSQKLSSASLRA
LDFSGNSLSQMWAEGDLYLCPFKGLRNLVQLDLSENHLHTLLPRHLDNLPKSLRQLRLRDNNLAFFNWSSLTVLP
RLEALDLAGNQLKALSNGSLPPGIRLQKLDVSSNSIGFVIPGFFVRATRLIELNLSANALKTVDPSWFGSLAGTL
KILDVSANPLHCACGAAFVDFLLERQEAVPGLSRRVTCGSPGQLQGRSIFTQDLRLCLDETLSLDCFG

SEQ ID NO:11 (Bovine TLR9)

30

50

gggaagtgggcgccaagcatccttccctgcagctgcctcccaacctgcccgccagaccctctggagaagccgcat $\verb|tccctgtcatgggcccctactgtgccccgcaccccctttctctctggtgcaggcggcactggcagcggccc| \\$ tggccgagggcaccctgcctgccttcctgccctgtgagctccagccccatggtcaggtggactgcaactggctgt tectgaagtetgtgeegeaetttteggetggageeeeegggeeaatgteaeeageeteteettaateteeaace qcatccaccacttgcatgactctgacttcgtccacctgtccaacctgcgggtcctcaacctcaagtggaactgcc cgccggccggcctcagccccatgcacttcccctgccgtatgaccatcgagcccaacaccttcctggctgtgccca $\verb|tggacggcaactgctactacatgaacccctgccggggccctggaggtggccccaggcgccctcctcggcctgg|$ gcaacctcacgcacctgtcgctcaagtacaacatctcacggaggtgcccqccqcctqcccccaqcctqqaca $\verb|ccctgctgctgtcctacaaccacattgtcaccctggcacccgaggacctggccaacctgactgccctgcgcgtgc|$ ttgacgtgggtgggaactgccgctgcgaccatgcccgcaacccctgcagggagtgcccaaagaacttcccca agetgeaccetgacacettcagtcacetgagecgeetcgaaggeetggtgttgaaggacaqttetetetacaaac tcaccaagaccaccatcttcaacgacctgacccagctgcgcagactcaacctgtccttcaattaccacaagaagg ${\tt tgtccttcgcccacctgcacctagcgtcctcctttgggagtctggtgtccctggagaagctggacatgcacggca}$ tettettecgeteceteaccaacateacgetecagtegetgacceggetgcccaagetecagagtetgcatetge ${\tt agctgaacttcatcaaccaggcccagctcagcatctttggggccttcccgagcctgctcttcgtggacctgtcgg}$ a caaccg cat cag cgg ag ccg ccg ccg cgc cctgg gg gag gt gg acag cag gg t gg aag tctgg cgattgcccaggggcctcgctccaggcccgctggacgccgtcagctcaaaggacttcatgccaagctgcaacctcaact tcaccttggacctgtcacggaacaacctggtgacaatccagcaagagatgtttacccgcctctcccgcctccagt gcctgcgcctgagccacaacagcatctcgcaggcggttaatggctcccagttcgtgccgctgaccagcctgcgag

tgctcgacctgtcccacaacaagctggacctgtaccatgggcgctcattcacggagctgccgcagctggaggcac tggacctcagctacaacagccagcccttcagcatgcagggcgtgggccacaacctcagcttcgtggcccagctgc cctccctgcgctacctcagccttgcgcacaatggcatccacagccgcgtgtcacagaagctcagcagcgcctcgt tgcgcgccctggacttcagcggcaactccctgagccagatgtgggccgaggggagacctctatctctgctttttca aaggettgaggaacetggtecagetggacetgtecgagaaceatetgcacacetectgcetegteacetggaca acctgcccaagagcctgcggcagctgcgtctccgggacaataacctggccttcttcaactggagcagcctgaccg tcctgccccggctggaagccctggatctggcaggaaaccagctgaaggccctgagcaacggcagcctgccgcctg gcatccggctccagaagctggacgtgagcagcaacagcatcggcttcgtgatccccggcttcttcgtccgcgcga $\verb|ctcggctgatagagcttaacctcagcgccaatgccctgaagacagtggatccctcctggttcggttccttagcag|$ $\tt ggaccctgaaaatcctagacgtgagcgccaacccgctccactgcgcctgcggggcggcctttgtggacttcctgc$ 10 tggagagacaggaggccgtgcccgggctgtccaggcgcgtcacatgtggcagtccgggccagctccagggccgca gcatcttcacacaggacctgcgcctctgcctggatgagaccctctccttggactgctttggcctctcactgctaa tggtggcgctgggcctggcagtgcccatgctgcaccacctctgtggctgggacctctggtactgcttccacctgt gtctggcccatttgccccgacggcggcggcagcggggaggacaccctgctctatgatgccgtcgtggtcttcg gggcgctccgcctctgcctggaggagcgagactggctccctggtaagacgctcttcgagaacctgtgggcctcgg ${\tt tctacagcagccgcaagaccatgttcgtgctggaccacacggaccgggtcagcggcctcctgcgcgccagcttcc}$ ggtcccgctacgtgcggctgcgccagcgctctgccgccagagcgtcctcctctggccccaccagcccagtggcc agggtagtttctgggccaacctgggcatagccctgaccagggacaaccgtcacttctataaccggaacttctgcc 20 ggggccccacgacagccgaatagcacagagtgactgcccag

SEQ ID NO:12 (Bovine TLR9)

atgggcccctactgtgccccgcaccccctttctctctctgtgcaggcggcggcactggcagcggccctggccgag ggcaccctgcctgccttcctgccctgtgagctccagccccatggtcaggtggactgcaactggctgttcctgaag 25 tctgtgccgcacttttcggctggagccccccgggccaatgtcaccagcctctccttaatctccaaccgcatccac cacttgcatgactctgacttcgtccacctgtccaacctgcgggtcctcaacctcaagtggaactgcccgccggcc ggcctcagccccatgcacttcccctgccgtatgaccatcgagcccaacacttcctggctgtgcccaccctggag 30 cacaccagcatcctggtgctaggcccacccacttcaccggcctgcacgccctgcgctttctgtacatggacggc aactgctactacatgaacccctgcccgcgggccctggaggtggccccaggcgccctcctcggcctgggcaacctc acgcacctgtcgctcaagtacaaccatcacggaggtgccccgccgcctgcccccagcctggacaccctgctg ctgtcctacaaccacattgtcaccctggcacccgaggacctggccaacctgactgccctgcgcgtgcttgacgtg ggtgggaactgccgccgctgcgaccatgcccgcaacccctgcagggagtgcccaaagaacttccccaagctgcac 35 cctgacaccttcagtcacctgagccgcctcgaaggcctggtgttgaaggacagttctctctacaaactagagaaa ${\tt accaccatcttcaacgacctgacccagctgcgcagactcaacctgtccttcaattaccacaagaaggtgtccttc}$ gcccacctgcacctagcgtcctcctttgggagtctggtgtccctggagaagctggacatgcacggcatcttcttc cgctccctcaccaacatcacgctccagtcgctgacccggctgcccaagctccagagtctgcatctgcagctgaac $\verb|tcatcaaccaggcccagctcagcatctttggggccttcccgagcctgctcttcgtggacctgtcggacaaccgc|$ ${\tt atcagcggagccgccgccctgggggaggtggacagcagggtggaagtctggcgattgcccagg}$ ggcctcgctccaggcccgctggacgccgtcagctcaaaggacttcatgccaagctgcaacctcaacttcaccttg gacctgtcacggaacaacctggtgacaatccagcaagagatgtttacccgcctctcccgcctccagtgcctgcgc $\verb|ctgagccacaacagcatctcgcaggcggttaatggctcccagttcgtgccgctgaccagcctgcgagtgctcgac| \\$ $\verb|ctgtcccacaacaagctggacctgtaccattgggcgctcattcacggagctgccgcagctggaggcactggacctc|$ $\verb|cgctacctcagccttgcgcacaatggcatccacagccgcgtgtcacagaagctcagcagcgcctcgttgcgcgcc|\\$ $\verb|ctggacttcagcggcaactccctgagccagatgtgggccgagggagacctctatctctgcttttcaaaggcttg|$ aggaacctggtccagctggacctgtccgagaaccatctgcacaccctcctgcctcgtcacctggacaacctgccc ${\tt aagagcctgcggcagctgcgtctccgggacaataacctggccttcttcaactggagcagcctgaccgtcctgccc}$ 50 $\verb|cggctggaagccttggaagccttgagcaacggcagccttggcatctgg|\\$ ${\tt atagagcttaacctcagcgccaatgccctgaagacagtggatccctcctggttcggttccttagcagggaccctg}$ aaaatcctagacgtgagcgccaacccgctccactgcgcctgcggggcggcctttgtggacttcctgctggagaga caggaggccgtgcccgggctgtccaggcgcgtcacatgtggcagtccggggccagctccagggccgcagcatcttc 55 acacaggacctgcgcctctgcctggatgagaccctctccttggactgctttggc

II. - II.

SEQ ID NO:13 (Equine TLR9)

 ${ t MGPCHGALQPLSLLVQAAMLAVALAQGTLPPFLPCELQPHGLVNCNWLFLKSVPHFSAAAPRDNVTSLSLLSNRI}$ HHLHDSDFAQLSNLQKLNLKWNCPPAGLSPMHFPCHMTIEPNTFLAVPTLEELNLSYNGITTVPALPSSLVSLIL ${\tt SRTNILQLDPTSLTGLHALRFLYMDGNCYYKNPCGRALEVAPGALLGLGNLTHLSLKYNNLTTVPRSLPPSLEYL}$ LLSYNHIVTLAPEDLANLTALRVLDVGGNCRRCDHARNPCVECPHKFPQLHSDTFSHLSRLEGLVLKDSSLYQLN PRWFRGLGNLTVLDLSENFLYDCITKTKAFQGLAQLRRLNLSFNYHKKVSFAHLTLAPSFGSLLSLQELDMHGIF FRSLSQKTLQPLARLPMLQRLYLQMNFINQAQLGIFKDFPGLRYIDLSDNRISGAVEPVATTGEVDGGKKVWLTS ${\tt RDLTPGPLDTPSSEDFMPSCKNLSFTLDLSRNNLVTVQPEMFAQLSRLQCLRLSHNSISQAVNGSQFVPLTSLQV}$ LDLSHNKLDLYHGRSFTELPRLEALDLSYNSQPFSMRGVGHNLSFVAQLPTLRYLSLAHNGIHSRVSQQLCSTSL 10 WALDFSGNSLSOMWAEGDLYLRFFQGLRSLIRLDLSQNRLHTLLPCTLGNLPKSLQLLRLRNNYLAFFNWSSLTL $\verb|LPNLETLDLAGNQLKALSNGSLPSGTQLQRLDVSRNSIIFVVPGFFALATRLRELNLSANALRTEEPSWFGFLAG|$ SLEVLDVSANPLHCACGAAFVDFLLQVQAAVPGLPSRVKCGSPGQLQGRSIFAQDLRLCLDKSLSWDCFGLSLLV VALGLAMPMLHHLCGWDLWYCFHLGLAWLPRRGWQRGADALSYDAFVVFDKAQSAVADWVYNELRVRLEERRGRR ALRLCLEERDWLPGKTLFENLWASVYSSRKMLFVLAHTDQVSGLLRASFLLAQQRLLEDRKDVVVLVILSPDARR 15 SRYVRLRQRLCRQSVLFWPHQPSGQRSFWAQLGMALTRDNRHFYNQNFCRGPTMAE

SEO ID NO:14 (Equine TLR9)

MGPCHGALQPLSLLVQAAMLAVALAQGTLPPFLPCELQPHGLVNCNWLFLKSVPHFSAAAPRDNVTSLSLLSNRI
HHLHDSDFAQLSNLQKLNLKWNCPPAGLSPMHFPCHMTIEPNTFLAVPTLEELNLSYNGITTVPALPSSLVSLIL
SRTNILQLDPTSLTGLHALRFLYMDGNCYYKNPCGRALEVAPGALLGLGNLTHLSLKYNNLTTVPRSLPPSLEYL
LLSYNHIVTLAPEDLANLTALRVLDVGGNCRRCDHARNPCVECPHKFPQLHSDTFSHLSRLEGLVLKDSSLYQLN
PRWFRGLGNLTVLDLSENFLYDCITKTKAFQGLAQLRRLNLSFNYHKKVSFAHLTLAPSFGSLLSLQELDMHGIF
FRSLSQKTLQPLARLPMLQRLYLQMNFINQAQLGIFKDFPGLRYIDLSDNRISGAVEPVATTGEVDGGKKVWLTS
RDLTPGPLDTPSSEDFMPSCKNLSFTLDLSRNNLVTVQPEMFAQLSRLQCLRLSHNSISQAVNGSQFVPLTSLQV
LDLSHNKLDLYHGRSFTELPRLEALDLSYNSQPFSMRGVGHNLSFVAQLPTLRYLSLAHNGIHSRVSQQLCSTSL
WALDFSGNSLSQMWAEGDLYLRFFQGLRSLIRLDLSQNRLHTLLPCTLGNLPKSLQLLRLRNNYLAFFNWSSLTL
LPNLETLDLAGNQLKALSNGSLPSGTQLQRLDVSRNSIIFVVPGFFALATRLRELNLSANALRTEEPSWFGFLAG
SLEVLDVSANPLHCACGAAFVDFLLQVQAAVPGLPSRVKCGSPGQLQGRSIFAQDLRLCLDKSLSWDCFG

SEQ ID NO:15 (Equine TLR9)

30

35

40

45

50

ctctgttctctgagctgttgccgcgtgaagggactgcgagcacaaagcatcctcctctgcagctgcccagtg tgccagctggaccctctggatcatctcccactccctgtcatgggcccttgccatggtgccctgcagcccctgtct ctcctggtgcaggcggccatgctggccgtggctctggcccaaggcaccctgcctcccttcctgccctgtgagctc cagccccacggcctggtgaactgcaactggctgttcctgaagtccgtgccccacttctcagcagcagcaccccgg gacaatgtcaccagcctttccttgctctccaaccgcatccaccacctccacgactccgactttgcccaactgtcc aacctgcagaaactcaacctcaaatggaactgcccgccagccggcctcagccccatgcacttcccctgccacatg accatcgagcccaacactttcctggctgtacccaccctggaggagctgaacctgagctacaacggcatcacgact gtgcctgccctgcccagctccctcgtgtccctgatcctgagccgcaccaacatcctgcagctagaccccaccagc acggtgccccgcagcctgcccctagcctggagtacctgctgttgtcctacaaccacattgtcaccctggcacct aacccctgcgtggagtgcccacataaattcccccagctgcactccgacaccttcagccacctaagccgcctagaa ggcctcgtgttgaaggatagttctctctaccagctgaaccccagatggttccgtggcctgggcaacctcacagtg ctcgacctgagtgagaacttcctctacgactgcatcaccaaaaccaaggcattccagggcctggcccagctgcga agactcaacttgtccttcaattaccataagaaggtgtccttcgcccacctgacgctggcaccctccttcgggagc qcccqcctgcccatgctccagcgtctgtatctgcagatgaacttcatcaaccaggcccagctcggcatcttcaag qacttccctggtctgcgctacatagacctgtcagacaaccgcatcagtggagctgtggagccggtggccaccaca ggggaggtggatggtgggaagaaggtctggctgacatccagggacctcactccaggcccactggacaccccagc tctgaggacttcatgccaagctgcaagaacctcagcttcaccttggacctgtcacggaacaacctggtaacagtc cagccagagatgtttgcccagctctcgcgcctccagtgcctgcgcctgagccacaacagcatctcgcaggcggtc

- 16 -

 $\verb|aatggctcacag| tcgtgccactgaccagcctgcaggtgctggacctgtcccataacaaactggacctgtaccat|$ ggtgtgggccacaacctcagctttgtggcccagctgcccaccctgcgctacctcagcctggcacacaatggcatc $\verb|cacagccgtgtgtcccagcagctctgcagcacctcgctgtgggccctggacttcagcggcaattccctgagccag|$ atgtgggctgagggagacctctatctccgcttcttccaaggcctgagaagcctaatccggctagacctgtcccag aatcgtctgcataccctcctgccatgcaccctgggcaacctccccaagagcttgcagctgctgcgtctccgtaac cagctgaaggctctgagcaatggcagcctgccttctggcacccagctccagaggctggacgtcagcaggaacagc atcatettegtggteeetggettetttgetetggeeaegaggetgegagageteaaeeteagtgeeaaegeeete aggacagaggagccctcctggtttggtttcctagcaggctcccttgaagtcctagatgtqagcgccaaccctctq cactgcgcctgtggggcagcctttgtggacttcctgctgcaggttcaggctgccgtgcctggtctgcccagccgc gtcaagtgtggcagtccgggccagctccagggccgcagcatcttcgcacaagacctgcgcctctgcctggacaag tccctctcctgggactgttttggtctctcattgctggttgtggccctgggcctggccatgcctatgttgcaccac $\verb|ctctgcggctgggacctctggtactgcttccacctgggcctggcctggctgccccggcggggtggcagcggggc|\\$ gcggatgccctgagctatgatgcctttgtggtcttcgacaaggcacagagcgcagtggccgactgggtgtacaat gaactgcgggtgcggctagaggagcgccgtgggcgccgggcgctccgcctgtgtctggaggagcgtgactggcta $\verb|cctggcaagacgctgttcgaaaacctgtgggcctcagtctacagcagccgcaagatgctgtttgtgcctggcccac|$ acggaccaggtcagtggcctcttgcgtgccagcttcctgctggcccagcagcgtctgctggaggaccgcaaggac gttgtggtgctggtaatcctgagccctgacgcccgccgttcccgttacgtgcggctgcgccagcgcctctqccqc cagagtgtcctcttctggccccaccagcctagtggccagcgcagcttctgggcccagctaggcatggccctgacc ${\tt agggacaaccgccacttctataaccagaacttctgccggggcccgacgatggctgagtagcacagagtgacagcc}$ tggcatgtacaacccccagccctgaccttgcctctctgcctatgatgcccagtctgcctcactctgtgacgccc tgctctgcctccgccaccctcacccctggcatacagcaggcactcaataaatgccactggcaggccaaacagcca aaaaaaaaaaaaa

25

30

35

40

45

50

55

15

20

SEQ ID NO:16 (Equine TLR9)

atgggcccttgccatggtgccctgcagcccctgtctctcctggtgcaggcggccatgctggccgtggctctggcc caaggcaccctgcctcccttcctgccctgtgagctccagccccacggcctggtgaactgcaactggctgttcctg aagtccgtgccccacttctcagcagcaccccgggacaatgtcaccagcctttccttgctctccaaccgcatc caccacctccacgactccgactttgcccaactgtccaacctgcagaaactcaacctcaaatggaactgcccgcca agccgcaccaacatcctgcagctagaccccaccagcctcacgggcctgcatgccctgcgcttcctatacatggat ggcaactgctactacaagaacccctgcgggcgggccctggaggtggccccaggcgccctccttggcctgggcaac $\verb|ctcacccacctgtcactcaagtacaacctcacaacggtgccccgcagcctgcccctagcctggagtacctg|$ ctgttgtcctacaaccacattgtcaccctggcacctgaggacctggccaatctgactgccctgcgtgtgctcgat gtgggtggaaactgccgccgctgtgaccatgcacgcaacccctgcgtggagtgcccacataaattcccccagctg $\verb|cactccgacaccttcagccacctaagccgcctagaaggcctcgtgttgaaggatagttctctctaccagctgaac| \\$ aaaaccaaggcattccagggcctggcccagctgcgaagactcaacttgtccttcaattaccataaqaagqtqtcc ttccgctcactcagccagaagacgctccagccactggcccgcctgcccatgctccagcgtctgtatctgcagatg ${\tt aacttcatcaaccaggcccagctcggcatcttcaaggacttccctggtctgcgctacatagacctgtcagacaac}$ $\verb|cgcatcagtggagctgtggagctggtggatggtggatggtggaagaaggtctggctgacatcc|\\$ ${\tt agggacctcactccaggcccactggacacccccagctctgaggacttcatgccaagctgcaagaacctcagcttc}$ ctgcgcctgagccacaacagcatctcgcaggcggtcaatggctcacagttcgtgccactgaccagcctgcaggtg ctggacctgtcccataacaaactggacctgtaccatgggcgctcgtttacggagctgccgcgactggaggccctg gacctcagctacaacagccagcccttcagcatgcggggtgtggggccacaacctcagctttgtggcccagctgccc accetgegetaceteageetggeacaeaatggeatecacageegtgtgteccageagetetgeageacetegetq tgggccctggacttcagcggcaattccctgagccagatgtgggctgagggagacctctatctccgcttcttccaa ggcctgagaagcctaatccggctagacctgtcccagaatcgtctgcataccctcctgccatgcaccctgggcaac $\verb|ctccccaagagcttgcagctgctccgtaacaattacctggccttcttcaattggagcagcctgaccctc|$ ${\tt acccagctccagaggctggacgtcagcaggaacagcatcatcttcgtggtccctggcttctttgctctggccacg}$ aggctgcgagagctcaacctcagtgccaacgccctcaggacagaggagccctcctggtttggtttcctagcaggc $\verb|tcccttgaagtcctagatgtgagcccaaccctctgcactgcgcctgtggggcagcctttgtggacttcctgctg|$

caggttcaggctgccgtgcctggtctgcccagccgcgtcaagtgtggcagtccgggccagctccagggccgcagcatcttcgcacaagacctgcgcctctgcctggacaagtccctctcctgggactgttttggt

SEQ ID NO:17 (Ovine TLR9)

MGPYCAPHPLSLLVQAAALAAALAQGTLPAFLPCELQPRGKVNCNWLFLKSVPRFSAGAPRANVTSLSLISNRIH
HLHDSDFVHLSNLRVLNLKWNCPPAGLSPMHFPCRMTIEPNTFLAVPTLEELNLSYNGITTVPALPSSLVSLSLS
RTSILVLGPTHFTGLHALRFLYMDGNCYYKNPCQQAVEVAPGALLGLGNLTHLSLKYNNLTEVPRRLPPSLDTLL
LSYNHIITLAPEDLANLTALRVLDVGGNCRCDHARNPCRECPKNFPKLHPDTFSHLSRLEGLVLKDSSLYKLEK
DWFRGLGRLQVLDLSENFLYDYITKTTIFRNLTQLRRLNLSFNYHKKVSFAHLQLAPSFGGLVSLEKLDMHGIFF
RSLTNTTLRPLTQLPKLQSLSLQLNFINQAELSIFGAFPSLLFVDLSDNRISGAARPVAALGEVDSGVEVWRWPR
GLAPGPLAAVSAKDFMPSCNLNFTLDLSRNNLVTIQQEMFTRLSRLQCLRLSHNSISQAVNGSQFVPLTRLRVLD
LSYNKLDLYHGRSFTELPQLEALDLSYNSQPFSMQGVGHNLSFVAQLPSLRYLSLAHNGIHSRVSQKLSSASLRA
LDFSGNSLSQMWAEGDLYLCFFKGLRNLVQLDLSKNHLHTTLPRHLDNLPKSLRQLRLRDNNLAFFNWSSLTVLP
QLEALDLAGNQLKALSNGSLPPGTRLQKLDVSSNSIGFVTPGFFVLANRLKELNLSANALKTVDPFWFGRLTETL
NILDVSANPLHCACGAAFVDFLLEMQAAVPGLSRRVTCGSPGQLQGRSIFAQDLRLCLDETLSLDCFGFSLLMVA
LGLAVPMLHHLCGWDLWYCFHLCLAHLPRRRQRGEDTLLYDAFVVFDKAQSAVADWVYNELRVQLEERRGRRAL
RLCLEERDWLPGKTLFENLWASVYSSRKTMFVLDHTDRVSGLLRASFLLAQQRLLEDRKDVVVLVILRPAAYRSR

YVRLRQRLCRQSVLLWPHQPSGQGSFWANLGMALTRDNRHFYNRNFCRGPTTAE

20 SEQ ID NO:18 (Ovine TLR9)

MGPYCAPHPLSLLVQAAALAAALAQGTLPAFLPCELQPRGKVNCNWLFLKSVPRFSAGAPRANVTSLSLISNRIH
HLHDSDFVHLSNLRVLNLKWNCPPAGLSPMHFPCRMTIEPNTFLAVPTLEELNLSYNGITTVPALPSSLVSLSLS
RTSILVLGPTHFTGLHALRFLYMDGNCYYKNPCQQAVEVAPGALLGLGNLTHLSLKYNNLTEVPRRLPPSLDTLL
LSYNHIITLAPEDLANLTALRVLDVGGNCRRCDHARNPCRECPKNFPKLHPDTFSHLSRLEGLVLKDSSLYKLEK
DWFRGLGRLQVLDLSENFLYDYITKTTIFRNLTQLRRLNLSFNYHKKVSFAHLQLAPSFGGLVSLEKLDMHGIFF
RSLTNTTLRPLTQLPKLQSLSLQLNFINQAELSIFGAFPSLLFVDLSDNRISGAARPVAALGEVDSGVEVWRWPR
GLAPGPLAAVSAKDFMPSCNLNFTLDLSRNNLVTIQQEMFTRLSRLQCLRLSHNSISQAVNGSQFVPLTRLRVLD
LSYNKLDLYHGRSFTELPQLEALDLSYNSQPFSMQGVGHNLSFVAQLPSLRYLSLAHNGIHSRVSQKLSSASLRA
LDFSGNSLSQMWAEGDLYLCFFKGLRNLVQLDLSKNHLHTLLPRHLDNLPKSLRQLRLRDNNLAFFNWSSLTVLP
30 QLEALDLAGNQLKALSNGSLPPGTRLQKLDVSSNSIGFVTPGFFVLANRLKELNLSANALKTVDPFWFGRLTETL
NILDVSANPLHCACGAAFVDFLLEMQAAVPGLSRRVTCGSPGOLOGRSIFAODLRLCLDETLSLDCFG

SEQ ID NO:19 (Ovine TLR9)

gtcggcacgggaagtgagcgccaagcatccttccctgcagctgccgcccaacttgcccgccagaccctctggaga 35 agccgcattccctgccatgggcccctactgtgccccgcaccccctttctctctggtgcaggcggcggcgctggc agcagccctggcccagggcaccctgcctgccttcctgccctgtgagctccagccccggggtaaggtgaactgcaa ctggctgttcctgaagtctgtgccgcgcttttcggccggagccccccgggccaatgtcaccagcctctccttaat ctccaaccgcatccaccacttgcacgactctgacttcgtccacctgtccaacctgcgggtcctcaacctcaagtg gaactgcccgccggcctcagccccatgcacttcccctgccgcatgaccatcgagcccaacaccttcctggc atecetgtegetgageegeaceageatectggtgetaggeeceaeceactteaceggeetgeacgeectgegett tetgtacatggaeggeaactgctactataagaacceetgeeageaggeegtggaggtggeeceaggegeeteet tggcctgggcaacctcacgcacctgtcgctcaagtacaacaacctcacggaggtgccccgccgcctgcccccag $\verb|cctggacaccctgctgctgctacaaccaccatcatcaccctggcacccgaggacctggccaatctgactgccct|\\$ gcgtgtgcttgatgtgggggggaactgccgccgctgcgaccacgcccgcaacccctgcagggagtgcccaaagaa cttccccaagctgcaccctgacaccttcagccacctgagccgcctcgaaggcctggtgttgaaggacagttctct tgactacatcaccaagaccaccatcttcaggaacctgacccagctgcgcagactcaacctgtccttcaattacca caagaaggtgtccttcgcccacctgcaactggcaccctcctttgggggcctggtgtccctggagaagctggacat gcacggcatcttcttccgctccctcaccaacaccacgctccggccgctgacccagctgcccaagctccagagtct gagtctgcagctgaacttcatcaaccaggccgagctcagcatcttttggggccttcccgagcctgctcttcgtgga cctgtcggacaaccgcatcagcggagctgcgaggccggtggccgccctcggggaggtggacagcggggtggaagt ctggcggtggcccaggggcctcgctcaggcccgctggccgccgtcagcgcaaaggacttcatgccaagctgcaa

-18-

cctcaacttcaccttggacctgtcacggaacaacctggtgacgatccagcaggagatgtttacccgcctctcccg $\verb|cctccagtgcctgagccacaacagcatctcgcaggctgtaatggctcgcagttcgtgccgctgacccg|$ cctgcgagtgctcgacctgtcctacaacaagctggacctgtaccatgggcgctcgttcacggagctgccgcagct $\tt ggaggcactggacctcagctacaacagccagcccttcagcatgcagggcgtgggccacaacctcagcttcgtggc$ ccagctgccgtccctgcgctacctcagccttgcgcacaacggcatccacagccgcgtgtcacagaagctcagcag cgcctcgctgcgcgccctggacttcagcggcaactccctgagccagatgtgggccgagggagacctctatctctg cttcttcaaaggcttgaggaacctggtccagctgtccaagaaccacctgcacacctcctgcctcgtca cctggataacctgcccaagagcctgcggcagctgcgtctccgggacaataacctggccttcttcaactggagcag $\verb|cctgactgttctgccccagctggaagccctggatctggcgggaaaccagctgaaggccctgagcaaccggcagcct| \\$ 10 ${\tt gccacctggcacccggctccagaagctggacgtgagcagcaacagcatcggctttgtgacccctggcttctttgt}$ ccttgccaaccggctgaaagagcttaacctcagcgccaacgccctgaagacagtggatcccttctggttcggtcg cttaacagagaccctgaatatcctagacgtgagcgccaacccgctccactgtgcctgcggggggcctttgtqqa cttcctgctggagatgcaggcggtgcctgggctgtccaggcgcgtcacgtgtggcagtccgggccagctcca $\tt gggccgcagcatcttcgcacaggacctgcgcctctgcctggatgagaccctctccttggactgcttttggcttctc$ 15 $\verb|gctgctaatggtggcgctgggcctggggtgcccatgctgcaccacctctgtggctgggacctgtggtactgctt|$ ccacctgtgtctggcccatttgccccgacggcggcggcagcggggcgaggacaccctgctctacgatgccttcgt ggtcttcgacaaggcgcagagtgcagtggccgactgggtgtacaacgagctccgcgtgcagctggaggagcgccg cgggcgccgggcgctccgcctctgcctggaggagcgagactggctccctggcaagacgctcttcgagaacctgtg $\verb|ggcctcggtctacagccgtaagaccatgttcgtgctggaccacacggaccgggtcagtggcctcctgcgcgc|$ 20 $\verb|cagcttcctgctggcccagcagcgcctgttggaggaccgcaaggatgtcgtggtgctggtgatcctgcgccccgc|\\$ $\verb|cgcctaccggtcccgctacgtgcgccagcgcctctgccgccagagcgtcctcctcttggccccaccagcc|\\$ cagtggccagggtagcttctgggccaacctgggcatggccctgaccagggacaaccgccacttctataaccggaa cttctgccggggcccacgacagccgaatagcacagagtgactgcccag

25 SEQ ID NO:20 (Ovine TLR9)

30

35

40

45

50

55

ggcaccctgccttcctgccctgtgagctccagcccggggtaaggtgaactgcaactggctgttcctgaag $\verb|tctgtgccgcgcttttcggccggagcccccgggccaatgtcaccagcctctccttaatctccaaccgcatccac|$ $\verb|cacttgcacgactctgacttcgtccacctgtccaacctgcgggtcctcaacctcaagtggaactgcccgccggcc|$ $\verb|ggcctcagccccatgcccttgccgcatgaccatcgagcccaacaccttcctggctgtgcccacccttggag|$ cgcaccagcatcctggtgctaggccccacccacttcaccggcctgcacgccctgcgctttctgtacatggacggc aactgctactataagaacccctgccagcaggccgtggaggtggccccaggcgccctccttggcctgggcaacctc acgcacctgtcgctcaagtacaaccacctcacggaggtgccccgccgcctgcccccagcctggacaccctgctg ggcgggaactgccgccgctgcgaccacgcccgcaacccctgcagggagtgcccaaagaacttccccaagctgcac cctgacaccttcagccacctgagccgcctcgaaggcctggtgttgaaggacagttctctctacaaactagagaaa accaccatcttcaggaacctgacccagctgcgcagactcaacctgtccttcaattaccacaagaaggtgtccttc ${\tt gcccacctgcaactggcaccctcctttgggggcctggtgtccctggagaagctggacatgcacggcatcttcttc}$ cgctccctcaccaacaccacgctccggccgctgacccagctgcccaagctccagagtctgagtctgcagctgaac ttcatcaaccaggccgagctcagcatctttggggccttcccgagcctgctcttcgtggacctgtcggacaaccgc atcagcggagctgcgaggccggtggcccctcggggaggtggacagcggggtggaagtctggcgggtggcccagg ggcctcgctccaggcccgctggccgccgtcagcgcaaaggacttcatgccaagctgcaacctcaacttcaccttg gacetgtcacggaacaacetggtgacgatccagcaggagatgtttacccgcctctcccgcctccagtgcctgcgc $\verb|ctgagccacaacagcatctcgcaggctgatcgcagttcgtgccgctgacccgcctgcgagtgctcgac| \\$ $\verb|ctgtcctacaacaagctggacctgtaccatgggcgctcgttcacggagctgccgcagctggaggcactggacctc|$ agctacaacagccagcccttcagcatgcagggcgtgggccacaacctcagcttcgtggcccagctgccgtccctg cgctacctcagccttgcgcacaacggcatccacagccgcgtgtcacagaagctcagcagcgcctcgctgcgcgcc ctggacttcagcggcaactccctgagccagatgtgggccgagggagacctctatctctgcttcttcaaaggcttg aggaacctggtccagctggacctgtccaagaaccacctgcacaccctcctgcctcgtcacctggataacctgccc aagageetgeggeagetgegteteegggacaataaeetggeettetteaaetggageageetgaetgttetgeee cagctggaagccctggatctggcgggaaaccagctgaaggccctgagcaacggcagcctgccacctggcacccgg ctccagaagctggacgtgagcagcaacagcatcggctttgtgacccctggcttcttttgtccttgccaaccggctg aaagagettaaeeteagegeeaaegeeetgaagaeagtggateeettetggtteggtegettaaeagagaeeetg aatateetagaegtgagegeeaaeeegeteeaetgtgeetgeggggeggeetttgtggaetteetgetggagatg

- 19 -

caggeggeegtgeetgggetgteeaggeggteacgtgtggeagteegggeeageteeagggeegeageatettegeacaggacetgegeetetgeetggatgagaceeteteettggaetgetttgge

Complete nucleotide and amino acid sequences for canine and feline TLR9 are publicly available. For example, an amino acid sequence for canine TLR9 is available as GenBank accession number BAC65192 and its corresponding nucleotide sequence is available as GenBank accession number AB104899. An amino acid sequence for feline TLR9 is available as GenBank accession number AAN15751 and its corresponding nucleotide sequence is available as GenBank accession number AY137581.

Complete nucleotide and amino acid sequences for canine and feline TLR9 were also determined independently from those available from public databases.

An amino acid sequence of canine TLR9 is provided as SEQ ID NO:21. Based on comparison with known amino acid sequences of human and murine TLR9, it appears that SEQ ID NO:21 includes sequence for at least a majority of the extracellular domain, all of the transmembrane domain, and at least a portion of the intracellular domain of canine TLR9 (See Figure 1). Amino acids numbered 1-822 of SEQ ID NO:21 are presumptively extracellular domain and correspond to SEQ ID NO:22. SEQ ID NO:23 is a nucleotide sequence of canine TLR9 cDNA having an open reading frame corresponding to nucleotides 91-3186. SEQ ID NO:24 is a nucleotide sequence of canine cDNA encoding amino acids 1-822 of SEQ ID NO:21.

An amino acid sequence of feline TLR9 is provided as SEQ ID NO:25. Based on comparison with known amino acid sequences of human and murine TLR9, it appears that SEQ ID NO:25 includes sequence for at least a majority of the extracellular domain, all of the transmembrane domain, and at least a portion of the intracellular domain of feline TLR9 (See Figure 1). Amino acids numbered 1-820 of SEQ ID NO:25 are presumptively extracellular domain and correspond to SEQ ID NO:26. SEQ ID NO:27 is a nucleotide sequence of feline TLR9 cDNA having an open reading frame corresponding to nucleotides 87-3179. SEQ ID NO:28 is a nucleotide sequence of feline cDNA encoding amino acids 1-820 of SEQ ID NO:25.

30

25

5

10

15

20

SEQ ID NO:21 (Canine TLR9)

MGPCRGALHPLSLLVQAAALALALAQGTLPAFLPCELQPHGLVNCNWLFLKSVPRFSAAAPRGNVTSLSLYSNRI HHLHDYDFVHFVHLRRLNLKWNCPPASLSPMHFPCHMTIEPNTFLAVPTLEDLNLSYNSITTVPALPSSLVSLSL SRTNILVLDPATLAGLYALRFLFLDGNCYYKNPCQQALQVAPGALLGLGNLTHLSLKYNNLTVVPRGLPPSLEYL

- 20 -

LLSYNHIITLAPEDLANLTALRVLDVGGNCRRCDHARNPCRECPKGFPQLHPNTFGHLSHLEGLVLRDSSLYSLD PRWFHGLGNLMVLDLSENFLYDCITKTKAFYGLARLRRLNLSFNYHKKVSFAHLHLASSFGSLLSLQELDIHGIF FRSLSKTTLQSLAHLPMLQRLHLQLNFISQAQLSIFGAFPGLRYVDLSDNRISGAAEPAAATGEVEADCGERVWP QSRDLALGPLGTPGSEAFMPSCRTLNFTLDLSRNNLVTVQPEMFVRLARLQCLGLSHNSISQAVNGSQFVPLSNL RVLDLSHNKLDLYHGRSFTELPRLEALDLSYNSQPFSMRGVGHNLSFVAQLPALRYLSLAHNGIHSRVSQQLRSA SLRALDFSGNTLSQMWAEGDLYLRFFQGLRSLVQLDLSQNRLHTLLPRNLDNLPKSLRLLRLRDNYLAFFNWSSL ALLPKLEALDLAGNQLKALSNGSLPNGTQLQRLDLSGNSIGFVVPSFFALAVRLRELNLSANALKTVEPSWFGSL AGALKVLDVTANPLHCACGATFVDFLLEVQAAVPGLPSRVKCGSPGQLQGRSIFAQDLRLCLDEALSWVCFSLSL LAVALSLAVPMLHQLCGWDLWYCFHLCLAWLPRRGRRRGVDALAYDAFVVFDKAQSSVADWVYNELRVQLEERRG RRALRLCLEERDWVPGKTLFENLWASVYSSRKTLFVLARTDRVSGLLRASFLLAQQRLLEDRKDVVVLVILCPDA HRSRYVRLRQRLCRQSVLLWPHQPSGQRSFWAQLGTALTRDNRHFYNQNFCRGPTTA

SEQ ID NO:22 (Canine TLR9)

10

15

20

25

30

35

40

45

50

55

MGPCRGALHPLSLLVQAAALALALAQGTLPAFLPCELQPHGLVNCNWLFLKSVPRFSAAAPRGNVTSLSLYSNRI
HHLHDYDFVHFVHLRRLNLKWNCPPASLSPMHFPCHMTIEPNTFLAVPTLEDLNLSYNSITTVPALPSSLVSLSL
SRTNILVLDPATLAGLYALRFLFLDGNCYYKNPCQQALQVAPGALLGLGNLTHLSLKYNNLTVVPRGLPPSLEYL
LLSYNHIITLAPEDLANLTALRVLDVGGNCRRCDHARNPCRECPKGFPQLHPNTFGHLSHLEGLVLRDSSLYSLD
PRWFHGLGNLMVLDLSENFLYDCITKTKAFYGLARLRRLNLSFNYHKKVSFAHLHLASSFGSLLSLQELDIHGIF
FRSLSKTTLQSLAHLPMLQRLHLQLNFISQAQLSIFGAFPGLRYVDLSDNRISGAAEPAAATGEVEADCGERVWP
QSRDLALGPLGTPGSEAFMPSCRTLNFTLDLSRNNLVTVQPEMFVRLARLQCLGLSHNSISQAVNGSQFVPLSNL
RVLDLSHNKLDLYHGRSFTELPRLEALDLSYNSQPFSMRGVGHNLSFVAQLPALRYLSLAHNGIHSRVSQQLRSA
SLRALDFSGNTLSQMWAEGDLYLRFFQGLRSLVQLDLSQNRLHTLLPRNLDNLPKSLRLLRLRDNYLAFFNWSSL
ALLPKLEALDLAGNQLKALSNGSLPNGTQLQRLDLSGNSIGFVVPSFFALAVRLRELNLSANALKTVEPSWFGSL
AGALKVLDVTANPLHCACGATFVDFLLEVQAAVPGLPSRVKCGSPGQLQGRSIFAQDLRLCLDEALSWVCFS

SEQ ID NO:23 (Canine TLR9)

aggaaggggctgtgagctccaagcatcctttcctgcagctgctgcccagcctgccagccctctggagaag ccccgctccctgtcatgggcccctgccgtggcgccctgcaccccctgtctctcctggtgcaggctgccgcgcta gccctggccctggcccagggcaccctgcctgccttcctgccctgtgagctccagccccatggcctggtgaactgc ${\tt aactggctgttcctcaagtccgtgccccgcttctcggcagctgcaccccgcggtaacgtcaccagcctttccttg}$ tactccaaccgcatccaccaccatcatgactatgactttgtccacttcgtccacctgcggcgtctcaatctcaag tggaactgcccgcccgccagcctcagccccatgcactttccctgtcacatgaccattgagcccaacaccttcctq gctgtgcccaccctagaggacctgaatctgagctataacagcatcacqactqtqcccqccctqcccaqttcqctt gtgtccctgtccctgagccgcaccaacatcctggtgctggaccctgccaccctggcaggcctttatgccctgcgc $\verb|ttcctgttcctggatggcaactgctactacaagaacccctgccagcaggccctgcaggtggccccaggtgccctc|$ $\verb|ctgggcctgggcaacctcacacctgtcactcaagtacaacaacctcaccgtggtgccgcgggggcctgccccc| \\$ ${\tt agcctggagtacctgctcttgtcctacaaccacatcatcaccctggcacctgaggacctggccaatctgactgcc}$ ctgcgtgtcctcgatgtgggtgggaactgtcgccgctgtgaccatgcccgtaacccctgcagggagtgccccaag ggcttcccccagctgcaccccaacaccttcggccacctgagccacctcgaaggcctggtgttgagggacagctct ${\tt tatgactgcatcaccaaaaccaaagccttctacggcctggcccggctgcgcagactcaacctgtccttcaattat}$ cataagaaggtgtcctttgcccacctgcatctggcatcctccttcgggagcctactgtccctgcaggagctggac atacatggcatcttcttccgctcgctcagcaagaccacgctccagtcgctggcccacctgcccatgctccagcgt ctgcatctgcagttgaactttatcagccaggcccagctcagcatcttcggcgccttccctqqactqcqqtacqtq gacttgtcagacaaccgcatcagtggagctgcagagcccgcggctgccacagggggaggtagaggcagactgtggg gagagagtetggccacagtcccgggaccttgctctgggcccactgggcacccccggctcagaggccttcatgccg ${\tt agctgcaggaccctcaacttcaccttggacctgtctcggaacaacctagtgactgttcagccggagatgtttgtc}$ cggctggcgcctccagtgcctgggcctgagccacaacagcatctcgcaggcggtcaatggctcgcagttcgtg cctctgagcaacctgcgggtgctggacctgtcccataacaagctggacctgtaccacgggcgctcgttcacggag agetttgtggcacagetgecagecetgegetacetcageetggegcacaatggcatecacageeggtgteecag cagctccgcagcgcctcgctccgggccctggacttcagtggcaataccctgagccagatgtgggccgagggagac ctctatctccgcttcttccaaggcctgagaagcctggttcagctggacctgtcccagaatcgcctgcataccctc ctgccacgcaacctggacaacctccccaagagcctgcggctcctgcggctccgtgacaattacctggctttcttc aactggagcagcctggccctcctacccaagctggaagccctggacctggcgggaaaccagctqaaggccctqagc

aatggcagettgcccaacggcacccagetccagaggetggacetcageggcaacagcateggettegtggtecee agcttttttgccctggccgtgaggcttcgagagctcaacctcagcgccaacgccctcaagacggtggagccctcc tggtttggttccctggcgggtgccctgaaagtcctagacgtgaccgccaaccccttgcattgcgcttgcgcgca ${\tt accttcgtggacttcttgctggaggtgcaggctgccggtcctgcctagccgtgtcaagtgcggcagcccg}$ ggccagetecagggccgcagcatettegcacaggacetgcgcctetgcctggacgaagcgctetectgggtetgt ttcagcctctcgctgctgtggccctgagcctggctgtgcccatgctgcaccagctctgtggctgggacctc gacgccttcgtggtcttcgacaaggcgcagagctcggtggcggactgggtgtacaatgagctgcgggtacagcta gaggagcgccgtgggcgccggggcgctacgcctgtgtctggaggaacgtgactgggtacccggcaaaaccctcttc $\tt gagaacctctgggcctcagtttacagcagccgcaagacgctgtttgtgctggcccgcacggacagagtcagcggc$ $\verb|ctcctgctgccagcttcctgctggcccaacagcgcctgctggaggaccgcaaggacgtcgtggtgctggtgatc|$ etgtgccccgacgcccaccgctcccgctatgtgcggctgcgccagcgcctctgccgccagagtgtcctcctctgg ccccaccagcccagtggccagcgcagcttctgggcccagctgggcacggccctgaccagggacaaccgccacttc tacaaccagaacttctgccggggccccacgacagcctgataggcagacagcccagcaccttcgcgcccctacacc 15 etgeetgtetgtetgggatgeeegaeetgetggetetaeaeegeegetetgteteeeetaeaeeeageeetggea taaagcgaccgctcaataaatgctgctggtagac

SEQ ID NO:24 (Canine TLR9)

atgggccctgccgtggcgcctgcacccctgtctctctggtgcaggctgccgcgctagccctggccctggcc 20 cagggcaccctgcctgccttcctgccctgtgagctccagccccatggcctggtgaactgcaactggctgttcctc aagtccgtgccccgcttctcggcagctgcaccccgcggtaacgtcaccagcctttccttgtactccaaccgcatc gccagcctcagccccatgcactttccctgtcacatgaccattgagcccaacaccttcctggctgtgcccacccta 25 agecgcaccaacatcctggtgctggaccctgccaccctggcaggcctttatgccctgcgcttcctggttcctggat ggcaactgctactacaagaacccctgccagcaggccctgcaggtggccccaggtgccctcctgggcctgggcaac ctcacacacctgtcactcaagtacaaccacctcaccgtggtgccgcgggggcctgcccccagcctggagtacctg ctcttgtcctacaaccaccatcatcaccctggcacctgaggacctggccaatctgactgccctgcgtgtcctcgat gtgggtgggaactgtcgccgctgtgaccatgcccgtaacccctgcagggagtgccccaagggcttcccccagctg 30 aaaaccaaagccttctacggcctggcccggctgcgcagactcaacctgtccttcaattatcataagaaggtgtcc ttccgctcgctcagcaagaccacgctccagtcgctggcccacctgcccatgctccagcgtctgcatctgcagttg 35 aactttatcagccaggcccagctcagcatcttcggcgccttccctggactgcggtacgtggacttgtcagacaac cgcatcagtggagctgcagagcccgcggctgccacaggggaggtagaggcagactgtggggagagagtctggcca cagtcccgggaccttgctctgggcccactgggcacccccggctcagaggccttcatgccgagctgcaggaccctc aacttcaccttggacctgtctcggaacaacctagtgactgttcagccggagatgtttgtccggctggcgcctc cagtgcctgggcctgagccacaacagcatctcgcaggcggtcaatggctcgcagttcgtgcctctgagcaacctg cgggtgctggacctgtcccataacaagctggacctgtaccacgggcgctcgttcacggagctgccgcggctggag gccttggacctcagctacaacagccagcccttcagcatgcggggcgtgggccacaatctcagctttgtggcacag ctgccagccctgcgctacctcagcctggcgcacaatggcatccacagccgcgtgtcccagcagctccgcagcgcc tegeteegggeeetggaetteagtggeaataecetgageeagatgtgggeegagggagaeetetateteegette ttccaaggcctgagaagcctggttcagctggacctgtcccagaatcgcctgcataccctcctgccacgcaacctg gacaacctccccaagagcctgcggctcctgcggctccgtgacaattacctggctttcttcaactggagcagcctg gccctcctacccaagctggaagccctggacctggcgggaaaccagctgaaggccctgagcaatggcagcttgccc aacggcacccagetccagaggctggacctcagcggcaacagcatcggcttcgtggtccccagctttttttgccctg gccgtgaggcttcgagagctcaacctcagcgccaacgccctcaagacggtggagccctcctggtttggttccctg gcgggtgccctgaaagtcctagacgtgaccgccaaccccttgcattgcgcttgcggcgcaaccttcgtggacttc 50 ttgetggaggtgeaggetgeggtgeecggeetgeetageegtgteaagtgeggeageecgggeeageteeaggge cgcagcatcttcgcacaggacctgcgcctctgcctggacgaagcgctctcctgggtctgtttcagc

100

۱۳. این

1

1.

4

 $i \in \mathbb{Z}$

SEQ ID NO:25 (Feline TLR9)

55

MGPCHGALHPLSLLVQAAALAVALAQGTLPAFLPCELQRHGLVNCDWLFLKSVPHFSAAAPRGNVTSLSLYSNRI HHLHDSDFVHLSSLRRLNLKWNCPPASLSPMHFPCHMTIEPHTFLAVPTLEELNLSYNSITTVPALPSSLVSLSL SRTNILVLDPANLAGLHSLRFLFLDGNCYYKNPCPQALQVAPGALLGLGNLTHLSLKYNNLTAVPRGLPPSLEYL
LLSYNHIITLAPEDLANLTALRVLDVGGNCRRCDHARNPCMECPKGFPHLHPDTFSHLNHLEGLVLKDSSLYNLN
PRWFHALGNLMVLDLSENFLYDCITKTTAFQGLAQLRRLNLSFNYHKKVSFAHLHLAPSFGSLLSLQQLDMHGIF
FRSLSETTLRSLVHLPMLQSLHLQMNFINQAQLSIFGAFPGLRYVDLSDNRISGAMELAAATGEVDGGERVRLPS
GDLALGPPGTPSSEGFMPGCKTLNFTLDLSRNNLVTIQPEMFARLSRLQCLLLSRNSISQAVNGSQFMPLTSLQV
LDLSHNKLDLYHGRSFTELPRLEALDLSYNSQPFSMQGVGHNLSFVAQLPALRYLSLAHNDIHSRVSQQLCSASL
RALDFSGNALSRMWAEGDLYLHFFRGLRSLVRLDLSQNRLHTLLPRTLDNLPKSLRLLRLRDNYLAFFNWSSLVL
LPRLEALDLAGNQLKALSNGSLPNGTQLQRLDLSSNSISFVASSFFALATRLRELNLSANALKTVEPSWFGSLAG
TLKVLDVTGNPLHCACGAAFVDFLLEVQAAVPGLPGHVKCGSPGQLQGRSIFAQDLRLCLDEALSWDCFGLSLLT
VALGLAVPMLHHLCGWDLWYCFHLCLAWLPRRGRRRGADALPYDAFVVFDKAQSAVADWVYNELRVRLEERRGRR
ALRLCLEERDWLPGKTLFENLWASVYSSRKMLFVLAHTDRVSGLLRASFLLAQQRLLEDRKDVVVLVILRPDAHR
SRYVRLRQRLCRQSVLLWPHQPSGQRSFWAQLGTALTRDNQHFYNQNFCRGPTTAE

SEQ ID NO:26 (Feline TLR9)

15 MGPCHGALHPLSLLVQAAALAVALAQGTLPAFLPCELQRHGLVNCDWLFLKSVPHFSAAAPRGNVTSLSLYSNRI
HHLHDSDFVHLSSLRRLNLKWNCPPASLSPMHFPCHMTIEPHTFLAVPTLEELNLSYNSITTVPALPSSLVSLSL
SRTNILVLDPANLAGLHSLRFLFLDGNCYYKNPCPQALQVAPGALLGLGNLTHLSLKYNNLTAVPRGLPPSLEYL
LLSYNHIITLAPEDLANLTALRVLDVGGNCRCDHARNPCMECPKGFPHLHPDTFSHLNHLEGLVLKDSSLYNLN
PRWFHALGNLMVLDLSENFLYDCITKTTAFQGLAQLRRLNLSFNYHKKVSFAHLHLAPSFGSLLSLQQLDMHGIF
FRSLSETTLRSLVHLPMLQSLHLQMNFINQAQLSIFGAFPGLRYVDLSDNRISGAMELAAATGEVDGGERVRLPS
GDLALGPPGTPSSEGFMPGCKTLNFTLDLSRNNLVTIQPEMFARLSRLQCLLLSRNSISQAVNGSQFMPLTSLQV
LDLSHNKLDLYHGRSFTELPRLEALDLSYNSQPFSMQGVGHNLSFVAQLPALRYLSLAHNDIHSRVSQQLCSASL
RALDFSGNALSRMWAEGDLYLHFFRGLRSLVRLDLSQNRLHTLLPRTLDNLPKSLRLRLRDNYLAFFNWSSLVL
LPRLEALDLAGNQLKALSNGSLPNGTQLQRLDLSSNSISFVASSFFALATRLRELNLSANALKTVEPSWFGSLAG
TLKVLDVTGNPLHCACGAAFVDFLLEVOAAVPGLPGHVKCGSPGOLOGRSIFAODLRLCLDEALSWDCFG

agggtctqcqaqctccaqqcattcttctctqccatcqctqcccaqtctqccatccaqaccctctqqaqaaqccc

SEQ ID NO:27 (Feline TLR9)

cactccctgtcatgggcccctgccatggcgccctgcaccccctgtctctcctggtgcaggctgccgcgctgqccq 30 tggccctggcccagggcaccctgcctttctgccctgtgagctccagcgccacggcctggtgaattgcgact ggctgttcctcaagtccgtgccccacttctcggcggcagcgcccgtggtaacgtcaccagcctttccctgtact ccaaccgcatccaccacctccacgactccgactttgtccacctgtccagcctgcggcgtctcaacctcaaatqqa actgcccacccgccagcctcagccccatgcacttcccctgtcacatgaccattgagccccacaccttcctggccg tgcccacctggaggagctgaacctgagctacaacagcatcacgacaqtacccgcctqcccagttccctcqtqt 35 ccctgtccttgagccgtaccaacatcctggtgctggaccctgccaacctcqcaggqctqcactccctqcqctttc tqttcctqqatqqcaactqctactacaaqaacccctqccqqaqqccctqcaqqtqqcccqqqqccctccttq gcctgggcaaccttacgcacctgtcactcaagtacaacaacctcactgcggtgccccgcggcctgcccccagcc tggagtacctgctattgtcctacaccacatcatcaccctqqcacctqqqccaacctqaccqccctqc gtgtgctcgatgtgggtgggaactgccgtcgctgtgaccacqcccqcaacccctgtatqqaqtqccccaaqqqct 40 actgcatcaccaaaaccacagccttccagggcctggcccaqctqcqcaqactcaacttqtctttcaattaccaca agaaggtgtcctttgcccacctgcatctggcgccctccttcggqaqcctqctctccctqcaqcaqctqqacatqc atggcatcttcttccgctcgctcagcgagaccacgctccggtcgctggtccacctgcccatgctccagagtctqc 45 acctgcagatgaacttcatcaatcaggcccagctcagcatcttcggggccttccctggcctgcgatacgtqqacc tgtcagacaaccgcataagtggagccatggagctggcggctgccacggggggaggtggatggtggggagagagtcc ggctgccatctggggacctagctctgggcccaccgggcacccctagctccgagggcttcatgccaggctgcaaga gcctccagtgcctgctcctgagccgcaacagcatctcqcaqqcaqtcaacqqctcacaatttatqccqctqacca 50 gcctgcaggtgctggacctgtcccataacaagctggacctgtaccatqqqqqctcttttcacqqaqctqccqcqqc tgqaqqccttggacctcagctacaacaqccagccettcagcatgcagggcgtgggtcacaacctcagctttgtgg cacagetqccqqcctqcqctatetcaqeetqqcqcacaacqacatecagagecqtqtqtcccaqcagetetqca gcgcctcgctgcgggccttggacttcagcggcaatgccttqagccqqatqtqqqccqagggagacctqtatctcc acttetteegaggeetgaggageetggteeggttggatetgteeagaategeetgeataceetettgeeaegea 55 ccctggacaacctccccaagagcctgcggctgctgcgtctccgtgacaattatctggctttcttcaactggagca

gcctggtcctcctccccaggctggaagccctggacctggcgggaaaccagctgaaggccctgagcaacggcagct tgcctaatggaacccagctccagaggctggacctcagcagcaacagtatcagcttcgtggcctccagctttttg ctctggccaccaggctgcgagagctcaacctcagtgccaacgccctcaagacggtggagccctcctggttcggtt ctctagcgggcaccctgaaagtcctagatgtgactggcaaccccttgcactgcgcctgtggggcggccttcgtgg acttcttgctggaggtgcaggctgcagtgccggcctgccaggccacgtcaagtgtggcagtccaggtcagctcc agggccgcagcatctttgcgcaggatctgcgcctctgcctggatgaggccctctcctgggactgttttggcctct cgctgctgaccgtggccctgggccgtgcccatgctgcaccacctctgtggctgggacctctggtactgct tggtcttcgacaaggcacagagcgcggtggccgactgggtgtacaacgagctgcgggtacggctagaggagcgcc gtggacgccgagcgctccgcctgtgcctggaggaacgtgactggctacccggtaaaacgctctttgagaacctgt $\verb|ccagctttctgctggcccagcagcgcctgctggaggaccgcaaggacgttgtggtgctggtgatcctgcgcccg|$ acgcccaccgctcccgctatgtgcggctgcgccagcgcctctgccgccagagcgtcctcctctggccccaccagc ccagtggccagcgcagcttctgggcccagctgggcacggccctgaccagggacaaccagcacttctataaccaga 15 acttctgccggggccccacgacggcagagtgaccgcccagcaccccaagcctcctacaccttgcctgtctgcctg ggatgccggg

SEQ ID NO:28 (Feline TLR9)

atgggcccctgccatggcgccctgcaccccctgtctctcctggtgcaggctgccgcgctggccgtggccctggcc cagggcaccctgcctgcctttctgccctgtgagctccagcgccacggcctggtgaattgcgactggctgttcctc 20 aagteegtgeeceaetteteggeggeagegeecegtggtaaegteaceageettteeetgtaeteeaacegeate caccacctccacgactccgactttgtccacctgtccagcctgcggcgtctcaacctcaaatggaactgcccaccc gccagcctcagccccatgcacttcccctgtcacatgaccattgagcccacaccttcctggccgtgcccaccctg gaggagetgaacetgagetacaacageatcacgacagtacccgccctgcccagttccctcgtgtccctgtccttg agccgtaccaacatcctggtgctggaccctgccaacctcgcagggctgcactccctgcgctttctgttcctggat ggcaactgctactacaagaacccctgcccgcaggccctgcaggtggccccgggcgccctccttggcctgggcaac cttacgcacctgtcactcaagtacaacaacctcactgcggtgccccgcgggcctgcccccagcctggagtacctq $\verb|ctattgtcctacaaccacatcatcaccctggccacctgaggacctggccaacctgaccgccctgcgtgtgctcgat|\\$ gtgggtgggaactgccgtcgctgtgaccacgcccgcaacccctgtatggagtgccccaagggcttcccgcacctg 30 aaaaccacagccttccagggcctggcccagctgcgcagactcaacttgtctttcaattaccacaagaaggtgtcc 35 aacttcatcaatcaggcccagctcagcatcttcggggccttccctggcctgcgatacgtggacctgtcagacaac cgcataagtggagccatggagctggcggctgccacgggggaggtggatggtgggggagagagtccggctgccatct ggggacctagctctgggcccaccgggcacccctagctccgagggcttcatgccaggctgcaagaccctcaacttc ctgctcctgagccgcaacagcatctcgcaggcagtcaacggctcacaatttatgccgctgaccagcctgcaggtg 40 ctggacctgtcccataacaagctggacctgtaccatgggcgctctttcacggagctgccgcggctggaggccctg gacctcagctacaacagccagcccttcagcatgcagggcgtgggtcacaacctcagctttgtggcacagctgccg gccctgcgctatctcagcctggcgcacaacgacatccacagccgtgtgtcccagcagctctgcagcgcctcgctg egggcettggacttcageggcaatgcettgageeggatgtgggeegagggagacetgtatetecaettetteega ggcctgaggagcctggtccggttggatctgtcccagaatcgcctgcataccctcttgccacgcaccctggacaac 45 ctccccaagagcctgcggctgctgcgtctccgtgacaattatctggctttcttcaactggagcagcctggtcctc ctccccaggctggaagccctggacctggcgggaaaccagctgaaggccctgagcaacggcagcttgcctaatgga acccagetccagaggctggacctcagcagcaacagtatcagcttcgtggcctccagettttttgctctggccacc aggctgcgagagctcaacctcagtgccaacgcctcaagacggtggagcctcctggttcggttctctagcgggc accetgaaagteetagatgtgactggcaaccecetgcactgcgcctgtggggcggccttcgtggacttcttgctg 50 gaggtgcaggctgcagtgccaggccacgtcaagtgtggcagtccaggtcagctccagggccgcagc atctttgcgcaggatctgcgctctgcctggatgaggccctctcctgggactgttttggc

٠,

Complete nucleotide and amino acid sequences for murine and human TLR9 are publicly available. For example, an amino acid sequence of murine TLR9 is available as

GenBank accession no. AAK29625, provided as SEQ ID NO:29. Amino acids numbered 1-821 of SEQ ID NO:29 presumptively include the entire extracellular domain and correspond to SEQ ID NO:30. SEQ ID NO:31 corresponds to GenBank accession number AF348140, which is a nucleotide sequence of murine TLR9 cDNA. SEQ ID NO:32 is a nucleotide sequence of murine cDNA encoding amino acids 1-821 of SEQ ID NO:29.

An amino acid sequence of human TLR9 is available as GenBank accession no. AAF78037, provided as SEQ ID NO:33. Amino acids numbered 1-820 of SEQ ID NO:33 presumptively include the entire extracellular domain and correspond to SEQ ID NO:34. SEQ ID NO:35 corresponds to GenBank accession number AF245704, which is a nucleotide sequence of human TLR9 cDNA. SEQ ID NO:36 is a nucleotide sequence of human cDNA encoding amino acids 1-820 of SEQ ID NO:33.

SEQ ID NO:29 (Murine TLR9)

MVLRRRTLHPLSLLVQAAVLAETLALGTLPAFLPCELKPHGLVDCNWLFLKSVPRFSAAASCSNITRLSLISNRI
HHLHNSDFVHLSNLRQLNLKWNCPPTGLSPLHFSCHMTIEPRTFLAMRTLEELNLSYNGITTVPRLPSSLVNLSL
SHTNILVLDANSLAGLYSLRVLFMDGNCYYKNPCTGAVKVTPGALLGLSNLTHLSLKYNNLTKVPRQLPPSLEYL
LVSYNLIVKLGPEDLANLTSLRVLDVGGNCRRCDHAPNPCIECGQKSLHLHPETFHHLSHLEGLVLKDSSLHTLN
SSWFQGLVNLSVLDLSENFLYESINHTNAFQNLTRLRKLNLSFNYRKKVSFARLHLASSFKNLVSLQELNMNGIF
FRSLNKYTLRWLADLPKLHTLHLQMNFINQAQLSIFGTFRALRFVDLSDNRISGPSTLSEATPEEADDAEQEELL
SADPHPAPLSTPASKNFMDRCKNFKFTMDLSRNNLVTIKPEMFVNLSRLQCLSLSHNSIAQAVNGSQFLPLTNLQ
VLDLSHNKLDLYHWKSFSELPQLQALDLSYNSQPFSMKGIGHNFSFVAHLSMLHSLSLAHNDIHTRVSSHLMSNS
VRFLDFSGNGMGRMWDEGGLYLHFFQGLSGLLKLDLSQNNLHILRPQNLDNLPKSLKLLSLRDNYLSFFNWTSLS
FLPNLEVLDLAGNQLKALTNGTLPNGTLLQKLDVSSNSIVSVVPAFFALAVELKEVNLSHNILKTVDRSWFGPIV
MNLTVLDVRSNPLHCACGAAFVDLLLEVQTKVPGLANGVKCGSPGQLQGRSIFAQDLRLCLDEVLSWDCFGLSLL
AVAVGMVVPILHHLCGWDVWYCFHLCLAWLPLLARSRRSAQALPYDAFVVFDKAQSAVADWVYNELRVRLEERRG
RRALRLCLEDRDWLPGQTLFENLWASIYGSRKTLFVLAHTDRVSGLLRTSFLLAQQRLLEDRKDVVVLVILRPDA
HRSRYVRLRQRLCRQSVLFWPQQPNGQGGFWAQLSTALTRDNRHFYNQNFCRGPTAE

SEQ ID NO:30 (Murine TLR9)

30 MVLRRRTLHPLSLLVQAAVLAETLALGTLPAFLPCELKPHGLVDCNWLFLKSVPRFSAAASCSNITRLSLISNRI
HHLHNSDFVHLSNLRQLNLKWNCPPTGLSPLHFSCHMTIEPRTFLAMRTLEELNLSYNGITTVPRLPSSLVNLSL
SHTNILVLDANSLAGLYSLRVLFMDGNCYYKNPCTGAVKVTPGALLGLSNLTHLSLKYNNLTKVPRQLPPSLEYL
LVSYNLIVKLGPEDLANLTSLRVLDVGGNCRRCDHAPNPCIECGQKSLHLHPETFHHLSHLEGLVLKDSSLHTLN
SSWFQGLVNLSVLDLSENFLYESINHTNAFQNLTRLRKLNLSFNYRKKVSFARLHLASSFKNLVSLQELNMNGIF
FRSLNKYTLRWLADLPKLHTLHLQMNFINQAQLSIFGTFRALRFVDLSDNRISGPSTLSEATPEEADDAEQEELL
SADPHPAPLSTPASKNFMDRCKNFKFTMDLSRNNLVTIKPEMFVNLSRLQCLSLSHNSIAQAVNGSQFLPLTNLQ
VLDLSHNKLDLYHWKSFSELPQLQALDLSYNSQPFSMKGIGHNFSFVAHLSMLHSLSLAHNDIHTRVSSHLNSNS
VRFLDFSGNGMGRMWDEGGLYLHFFQGLSGLLKLDLSQNNLHILRPQNLDNLPKSLKLLSLRDNYLSFFNWTSLS
FLPNLEVLDLAGNQLKALTNGTLPNGTLLQKLDVSSNSIVSVVPAFFALAVELKEVNLSHNILKTVDRSWFGPIV
MNLTVLDVRSNPLHCACGAAFVDLLLEVQTKVPGLANGVKCGSPGQLQGRSIFAQDLRLCLDEVLSWDCFG

SEQ ID NO:31 (Murine TLR9)

tgtcagagggagcctcgggagaatcctccatctcccaacatggttctccgtcgaaggactctgcacccttgtccctcctggtacaggctgcagtgctggagactctggccctgggtaccctgcctqccttcctaccctqtqaqctq

44

Ť

aagceteatggeetggtggaetgeaattggetgtteetgaagtetgtaeeeegtttetetgeggeageateetge tccaacatcacccgcctctccttgatctccaaccgtatccaccacctgcacaactccgacttcgtccacctgtcc ${\tt accattgagcccagaaccttcctggctatgcgtacactggaggagctgaacctgagctataatggtatcaccact}$ gtgccccgactgcccagctccctggtgaatctgagcctgagccacaccaacatcctggttctagatgctaacagc ctcgccggcctatacagcctgcgcgttctcttcatggacgggaactgctactacaagaacccctgcacaggagcg gtgaaggtgaccccaggcgccctcctgggcctgagcaatctcacccatctgtctctgaagtataacaacctcaca aaggtgccccgccaactgcccccagcctggagtacctcctggtgtcctataacctcattgtcaagctggggcct ${\tt aatccctgtatagaatgtggccaaaagtccctccacctgcaccctgagaccttccatcacctgagccatctggaa}$ $\tt ggcctggtgctgaaggacagctctccatacactgaactcttcctggttccaaggtctggtcaacctctcggtg$ ctggacctaagcgagaactttctctatgaaagcatcaaccaccactgcctttcagaacctaacccgcctgcgc ${\tt aagctcaacctgtccttcaattaccgcaagaaggtatcctttgcccgcctccacctggcaagttccttcaagaac}$ gccgatctgcccaaactccacactctgcatcttcaaatgaacttcatcaaccaggcacagctcagcatctttggt ${\tt accttccgagcccttcgctttgtggacttgtcagacaatcgcatcagtgggccttcaacgctgtcagaagccacc}$ $\verb|cctgaagaggaggaggaggaggaggaggtgttgtctgcggatcctcacccagctccactgagcacccct| \\$ gcttctaagaacttcatggacaggtgtaagaacttcaagttcaccatggacctgtctcggaacaacctggtgact atcaagccagagatgtttgtcaatctctcacgcctccagtgtcttagcctgagccacaactccattgcacaggct 20 gtcaatggctctcagttcctgccgctgactaatctgcaggtgctggacctgtcccataacaaactggacttgtac aagggtataggccacaatttcagttttgtggcccatctgtccatgctacacagccttagcctggcacacaatgac attcatacccgtgtgtcctcacatctcaacagcaactcagtgaggtttcttgacttcagcggcaacggtatgggc cgcatgtgggatgaggggggcctttatctccatttcttccaaggcctgagtggcctgctgaagctggacctgtct caaaataacctgcatatcctccggccccagaaccttgacaacctccccaagagcctgaagctgctgagcctccga aaccagctaaaggccctgaccaatggcaccctgcctaatggcaccctcctccagaaactggatgtcagcagcaac agtatcgtctctgtggtcccagccttcttcgctctggcggtcgagctgaaagaggtcaacctcagccacaacatt ctcaagacggtggatcgctcctggtttgggcccattgtgatgaacctgacagttctagacgtgagaagcaaccct 30 ctgcactgtgcctgtggggcagccttcgtagacttactgttggaggtgcagaccaaggtgcctggcctggctaat ggtgtgaagtgtggcagcccggccagctgcagggccgtagcatcttcgcacaggacctgcggctgtgcctggat gaggtcctctcttgggactgctttggcctttcactcttggctgtggccgtgggcatggtggtgcctatactgcac catctctgcggctgggacgtctggtactgttttcatctgtgcctggcatggctacctttgctggcccgcagccga cgcagcgcccaagctctcccctatgatgccttcgtggtgttcgataaggcacagagcgcagttgcggactgggtg tataacgagctgcgggtgcggctggaggagcgggcgcggtcgccgagccctacgcttgtgtctggaggaccgagat tggctgcctggccagacgctcttcgagaacctctgggcttccatctatgggagccgcaagactctatttgtgctg geccaeaeggaeegegteagtggeeteetgegeaeeagetteetgetggeteageagegeetgttggaagaeege ${\tt aaggacgtggtgttggtgatcctgcgtccggatgcccaccgctcccgctatgtgcgactgcgccagcgtctc}$ tgccgccagagtgtgctcttctggccccagcagcccaacgggcaggggggcttctgggcccagctgagtacagcc 40 ctgactagggacaaccgccacttctataaccagaacttctgccggggacctacagcagaatagctcagagcaaca

SEQ ID NO:31 (Murine TLR9)

45 ctgggtaccctgcctgcctaccctgtgagctgaagcctcatggcctggtggactgcaattggctgttcctg aagtetgtaeeeegtttetetgeggeageateetgeteeaacateaeeegeeteteettgateteeaaeegtate caccacctgcacaactccgacttcgtccacctgtccaacctgcggcagctgaacctcaagtggaactgtccaccc actggccttagccccctgcacttctcttgccacatgaccattgagcccagaaccttcctggctatgcgtacactg gaggagetgaacetgagetataatggtateaceactgtgeecegaetgeecageteeetggtgaatetgageetg 50 agccacaccaacatcctggttctagatgctaacagcctcgccggcctatacagcctgcgcgttctcttcatggac gggaactgctactacaagaacccctgcacaggagcggtgaaggtgaccccaggcgccctcctgggcctgagcaat ctcacccatctgtctctgaagtataacaacctcacaaaggtgccccgccaactgcccccagcctggagtacctc ctggtgtcctataacctcattgtcaagctggggcctgaagacctggccaatctgacctcccttcgagtacttgat gtgggtgggaattgccgtcgctgcgaccatgccccaatccctgtatagaatgtggccaaaagtccctccacctg 55 caccctgagaccttccatcacctgagccatctggaaggcctggtgctgaaggacagctctctccatacactgaac tetteetggtteeaaggtetggteaaceteteggtgetggaeetaagegagaaetttetetatgaaageateaae cacaccaatgeetttcagaacctaaccegeetgegeaagetcaacetgteettcaattacegeaagaaggtatee

tttgcccgcctccacctggcaagttccttcaagaacctggtgtcactgcaggagctgaacatgaacggcatcttc ttccgctcgctcaacaagtacacgctcagatggctggccgatctgcccaaactccacactctgcatcttcaaatg aacttcatcaaccaggcacagctcagcatctttggtaccttccgagcccttcgctttgtggacttgtcagacaat cgcatcagtgggccttcaacgctgtcagaagccacccctgaagaggcagatgatgcagagcaggaggaggtgttg tctqcqqatcctcacccaqctccactqaqcacccctqcttctaaqaacttcatqqacaqqtqtaaqaacttcaaq ttcaccatqqacctqtctcqqaacaacctqqtqactatcaaqccaqaqatqtttqtcaatctctcacqcctccaq tgtcttagcctgagccacaactccattgcacaggctgtcaatggctctcagttcctgccgctgactaatctgcag gtgctggacctgtcccataacaaactggacttgtaccactggaaatcgttcagtgagctaccacagttgcaggcc ctggacctgagctacaacagccagccctttagcatgaagggtataggccacaatttcagttttgtggcccatctg tccatgctacacagccttagcctggcacacaatgacattcatacccgtgtgtcctcacatctcaacagcaactca gtgaggtttcttgacttcagcggcaacggtatgggccgcatgtgggatgaggggggcctttatctccatttcttc caaggcctgagtggcctgctgaagctggacctgtctcaaaataacctgcatatcctccggccccagaaccttgac ttcctgcccaacctggaagtcctagacctggcaggcaaccagctaaaggccctgaccaatggcaccctgcctaat qqcaccctcctccaqaaactqqatqtcaqcaqcaacaqtatcqtctctqtqqtcccaqccttcttcqctctqqcq gtcgagctgaaagaggtcaacctcagccacaacattctcaagacggtggatcgctcctggtttgggcccattgtg atgaacctgacagttctagacgtgagaagcaaccctctgcactgtgcctgtggggcagccttcgtagacttactg ttggaggtgcagaccaaggtgcctggcctggctaatggtgtgaagtgtggcagccccggccagctgcaggccgt agcatcttcqcacaqqacctqcqqctqtqcctqqatqaqqtcctctctttqqqactqcttttqqc

20

40

45

10

15

SEQ ID NO:33 (Human TLR9)

MGFCRSALHPLSLLVOAIMLAMTLALGTLPAFLPCELOPHGLVNCNWLFLKSVPHFSMAAPRGNVTSLSLSSNRI HHLHDSDFAHLPSLRHLNLKWNCPPVGLSPMHFPCHMTIEPSTFLAVPTLEELNLSYNNIMTVPALPKSLISLSL SHTNILMLDSASLAGLHALRFLFMDGNCYYKNPCRQALEVAPGALLGLGNLTHLSLKYNNLTVVPRNLPSSLEYL 25 LLSYNRIVKLAPEDLANLTALRVLDVGGNCRRCDHAPNPCMECPRHFPQLHPDTFSHLSRLEGLVLKDSSLSWLN ASWFRGLGNLRVLDLSENFLYKCITKTKAFQGLTQLRKLNLSFNYQKRVSFAHLSLAPSFGSLVALKELDMHGIF FRSLDETTLRPLARLPMLQTLRLQMNFINQAQLGIFRAFPGLRYVDLSDNRISGASELTATMGEADGGEKVWLQP GDLAPAPVDTPSSEDFRPNCSTLNFTLDLSRNNLVTVQPEMFAQLSHLQCLRLSHNCISQAVNGSQFLPLTGLQV LDLSRNKLDLYHEHSFTELPRLEALDLSYNSQPFGMQGVGHNFSFVAHLRTLRHLSLAHNNIHSQVSQQLCSTSL 30 RALDFSGNALGHMWAEGDLYLHFFQGLSGLIWLDLSQNRLHTLLPQTLRNLPKSLQVLRLRDNYLAFFKWWSLHF LPKLEVLDLAGNRLKALTNGSLPAGTRLRRLDVSCNSISFVAPGFFSKAKELRELNLSANALKTVDHSWFGPLAS ALQILDVSANPLHCACGAAFMDFLLEVQAAVPGLPSRVKCGSPGQLQGLSIFAQDLRLCLDEALSWDCFALSLLA VALGLGVPMLHHLCGWDLWYCFHLCLAWLPWRGROSGRDEDALPYDAFVVFDKTOSAVADWVYNELRGOLEECRG RWALRLCLEERDWLPGKTLFENLWASVYGSRKTLFVLAHTDRVSGLLRASFLLAQORLLEDRKDVVVLVILSPDG 35 RRSRYVRLRQRLCRQSVLLWPHQPSGQRSFWAQLGMALTRDNHHFYNRNFCQGPTAE

SEQ ID NO:34 (Human TLR9)

MGFCRSALHPLSLLVQAIMLAMTLALGTLPAFLPCELQPHGLVNCNWLFLKSVPHFSMAAPRGNVTSLSLSSNRI
HHLHDSDFAHLPSLRHLNLKWNCPPVGLSPMHFPCHMTIEPSTFLAVPTLEELNLSYNNIMTVPALPKSLISLS
SHTNILMLDSASLAGLHALRFLFMDGNCYYKNPCRQALEVAPGALLGLGNLTHLSLKYNNLTVVPRNLPSSLEYL
LLSYNRIVKLAPEDLANLTALRVLDVGGNCRRCDHAPNPCMECPRHFPQLHPDTFSHLSRLEGLVLKDSSLSWLN
ASWFRGLGNLRVLDLSENFLYKCITKTKAFQGLTQLRKLNLSFNYQKRVSFAHLSLAPSFGSLVALKELDMHGIF
FRSLDETTLRPLARLPMLQTLRLQMNFINQAQLGIFRAFPGLRYVDLSDNRISGASELTATMGEADGGEKVWLQP
GDLAPAPVDTPSSEDFRPNCSTLNFTLDLSRNNLVTVQPEMFAQLSHLQCLRLSHNCISQAVNGSQFLPLTGLQV
LDLSRNKLDLYHEHSFTELPRLEALDLSYNSQPFGMQGVGHNFSFVAHLRTLRHLSLAHNNIHSQVSQQLCSTSL
RALDFSGNALGHMWAEGDLYLHFFQGLSGLIWLDLSQNRLHTLLPQTLRNLPKSLQVLRLRDNYLAFFKWWSLHF
LPKLEVLDLAGNRLKALTNGSLPAGTRLRRLDVSCNSISFVAPGFFSKAKELRELNLSANALKTVDHSWFGPLAS
ALQILDVSANPLHCACGAAFMDFLLEVQAAVPGLPSRVKCGSPGQLQGLSIFAQDLRLCLDEALSWDCFA

50 SEO ID NO:35 (Human TLR9)

aggetggtataaaaatettaetteetetattetetgageegetgetgeeetgtggggaagggaeetegagtgtga ageateetteeetgtagetgetgteeagtetgeeegeeagaeeetetggagaageeeetgeeeeeageatgggt ttetgeegeagegeeetgeaceegetgteteteetggtgeaggeeateatgetggeeatgaeeetggeeetggg

accttgcctgccttcctaccctgtgagctccagccccacggcctggtgaactgcaactggctgttcctgaagtct gtgccccacttctccatggcagcaccccgtggcaatgtcaccagcctttccttgtcctccaaccgcatccaccac $\verb"ctccatgattctgactttgcccaccttgcccagcctgcgcatctcaacctcaagtggaactgcccgccggttggc"$ $\verb|ctcagecccatgcacttcccctgccacatgaccatcgagcccagcaccttcttggctgtgcccaccctggaagag|$ ctaaacctgagctacaacaacatcatgactgtgcctgcgctgcccaaatccctcatatccctgtccctcagccat accaacateetgatgetagaetetgecageetegeeggeetgeatgeeetgegetteetatteatggaeggeaac ${\tt tgttattacaagaacccctgcaggcaggcactggaggtggccccgggtgccctccttggcctgggcaacctcacc}$ cacctgtcactcaagtacaacaacctcactgtggtgccccgcaacctgccttccagcctggagtatctgctgttg ${\tt tcctacaaccgcatcgtcaaactggcgcctgaggacctggccaatctgaccgccctgcgtgtgctcgatgtgggc}$ ggaaattgccgccgctgcgaccacgctcccaacccctgcatggagtgccctcgtcacttcccccagctacatccc gatacettcagecacetgagecgtettgaaggeetggtgttgaaggacagttetetetetetggetgaatgecagt ${\tt aaggccttccagggcctaacacagctgogcaagcttaacctgtccttcaattaccaaaagagggtgtcctttgcc}$ $\verb|cacctgtctctggcccttccttcgggagcctggtcgccctgaaggagctggacatgcacggcatcttcttccgc|$ tcactcgatgagaccacgctccggccactggcccgcctgcccatgctccagactctgcgtctgcagatgaacttc 15 atcaaccaggcccagctcggcatcttcagggccttccctggcctgcgctacgtggacctgtcggacaaccgcatc agcggagcttcggagctgacagccaccatgggggaggcagatggaggggagaaggtctggctgcagcctggggac cttgctccggccccagtggacactcccagctctgaagacttcaggcccaactgcagcaccctcaacttcaccttg gatetgteacggaacaacetggtgacegtgcageeggagatgtttgeecagetetegeacetgeagtgeetgege ctgagccacaactgcatctcgcaggcagtcaatggctcccagttcctgccgctgaccggtctgcaggtgctagac 20 ctqtcccqcaataagctggacctctaccacgagcactcattcacggagctaccgcgactggaggccctggacctc agctacaacagccagccctttggcatgcagggcgtgggccacaacttcagcttcgtggctcacctgcgcaccctg cqccacctcaqcctqqcccacaacaacatccacagccaagtgtcccagcagctctgcagtacgtcgctgcgggcc ctqqacttcaqcqqcaatqcactggqccatatqtgggccgaggggagacctctatctgcacttcttccaaggcctg 25 agcggtttgatctggctggacttgtcccagaaccgcctgcacaccctcctgccccaaaccctgcgcaacctcccc aagagcctacaggtgctgcgtctccgtgacaattacctggccttctttaagtggtggagcctccacttcctgccc aaactggaagteetegacetggcaggaaaceggetgaaggeeetgaceaatggcageetgeetgetggcaceegg ctccggaggctggatgtcagctgcaacagcatcagcttcgtggcccccggcttcttttccaaggccaaggagctg cgagagctcaaccttagcgccaacgccctcaagacagtggaccactcctggtttgggcccctggcgagtgccctg caaatactagatgtaagcgccaaccctctgcactgcgcctgtggggcggcctttatggacttcctgctggaggtg 30 caggetgeegtgeeeggtetgeeeageegggtgaagtgtggeagteegggeeageteeagggeeteageatettt ctgggcctgggtgtgcccatgctgcatcacctctgtggctgggacctctggtactgcttccacctgtgcctggcc tggcttccctggcggggggggcaaagtgggcgagatgaggatgccctgccctacgatgccttcgtggtcttcgac aaaacgcagagcgcagtggcagactgggtgtacaacgagcttcgggggcagctggaggagtgccgtgggcgctgg 35 gcactccgcctgtgcctggaggaacgcgactggctgcctggcaaaaccctctttgagaacctgtgggcctcggtc tatggcagccgcaagacgctgtttgtgctggcccacacggaccgggtcagtggtctctttgcgcgccagcttcctg $\verb|ctggcccagcagcgcctgctggaggaccgcaaggacgtcgtggtgctggtgatcctgagccctgacggccgccgc| \\$ $\verb|tcccgctacgtgcgcctgcgccagcgcctctgccgccagagtgtcctcctctggccccaccagcccagtggtcag|$ $\verb|cgcag| \verb|ctctgggcccagctgggcatggccctgaccagggacaaccaccacttctataaccggaacttctgccag|$ 40 tggtctgaccctccctgctcgcctccctcaccccacacctgacacagagca

SEQ ID NO:36 (Human TLR9)

- 28 -

aaaaccaaggccttccagggcctaacacagctgcgcaagcttaacctgtccttcaattaccaaaagagggtgtcc tttgcccacctgtctctggccccttccttcgggagcctggtcgccctgaaggagctggacatgcacggcatcttc ttccgctcactcgatgagaccacgctccggccactggcccgcctgcccatgctccagactctgcgtctgcagatg aacttcatcaaccaggcccagctcggcatcttcagggccttccctggcctgcgctacgtggacctgtcggacaac cgcatcagcggagcttcggagctgacagccaccatgggggaggcagatggaggggagaaggtctggctgcagcct ggggaccttgctccggccccagtggacactcccagctctgaagacttcaggcccaactgcagcaccctcaacttc accttggatctgtcacggaacaacctggtgaccgtgcagccggagatgtttgcccagctctcgcacctgcagtgc etgegeetgageeacaaetgeatetegeaggeagteaatggeteecagtteetgeegetgaeeggtetgeaggtg $\verb|ctagacctgtcccgcaataagctggacctctaccacgagcactcattcacggagctaccgcgactggaggccctg|$ gaceteagetacaacagecagecetttggcatgcagggcgtgggccacaaettcagettcgtggctcacetgcgc accetgegeeaccteageetggeecacaacaacatecacagecaagtgteecageagetetgeagtacgtegetg $\verb|cgggccctggacttcagcggcaatgcactgggccatatgtgggccgagggagacctctatctgcacttcttccaa|\\$ ggcctgagcggtttgatctggcttggacttgtcccagaaccgcctgcacaccctcctgccccaaaccctgcgcaac ctccccaaqagcctacaggtgctgcgtctccgtgacaattacctqgccttctttaagtqqtqqaqcctccacttc accoggetccggaggetggatgtcagctgcaacagcatcagcttcgtggcccccggcttcttttccaaggccaag gagctgcgagagctcaaccttagcgccaacgccctcaagacagtggaccactcctggtttgggcccctggcgagt gaggtgcaggctgccgtgcccggtctgcccagccgggtgaagtgtggcagtccgggccagctccagggcctcagc atctttgcacaggacctgcgctctgcctggatgaggccctctcctgggactgtttcgcc

10

15

20

25

30

35

In addition to the foregoing native rat, porcine, bovine, equine, and ovine TLR9 polypeptides and nucleic acid molecules encoding them, chimeric TLR9 polypeptides and nucleic acid molecules encoding them are provided by the invention. The chimeric polypeptides include at least one amino acid substitution based on a comparison of conserved and non-conserved amino acids among at least two of rat, murine, porcine, bovine, equine, ovine, canine, feline, and human TLR9. The information contained in a multiple sequence alignment of these various TLR9 polypeptide sequences, provided for example in Figure 1, can be used to identify and select individual amino acid positions and even individual amino acids to substitute in designing a chimeric TLR9. The substitution or substitutions can be effected using methods known to those of ordinary skill in molecular biology. Nucleic acids encoding the native or chimeric polypeptides of the invention can be inserted into an expression vector and used to express TLR9 polypeptide.

A conservative amino acid substitution shall refer to a substitution of a first amino acid for a second amino acid, wherein side chains of the first amino acid and the second amino acid share similar features in terms of hydrophobicity, size, aromaticity, or tendency to alter conformation. For example, conservative amino acid substitutions generally may be made between members within each of the following groups: hydrophobic (A, I, L, M, V), neutral (C, S, T), acidic (D, E), basic (H, K, N, Q, R), and aromatic (F, W, Y). A non-conservative amino acid substitution refers to any other amino acid substitution.

An expression vector for TLR9 will include at least a nucleotide sequence coding for a TLR9, or a fragment thereof coding for a functional TLR9 polypeptide, operably linked to a gene expression sequence which can direct the expression of the TLR9 nucleic acid within a eukaryotic or prokaryotic cell. A "gene expression sequence" is any regulatory nucleotide sequence, such as a promoter sequence or promoter-enhancer combination, which facilitates the efficient transcription and translation of the nucleic acid to which it is operably linked. With respect to TLR9 nucleic acid, the "gene expression sequence" is any regulatory nucleotide sequence, such as a promoter sequence or promoter-enhancer combination, which facilitates the efficient transcription and translation of the TLR9 nucleic acid to which it is operably linked. The gene expression sequence may, for example, be a mammalian or viral promoter, such as a constitutive or inducible promoter. Constitutive mammalian promoters include, but are not limited to, the promoters for the following genes: hypoxanthine phosphoribosyl transferase (HPRT), adenosine deaminase, pyruvate kinase, β-actin promoter, and other constitutive promoters. Exemplary viral promoters which function constitutively in eukaryotic cells include, for example, promoters from the simian virus (e.g., SV40), papillomavirus, adenovirus, human immunodeficiency virus (HIV), Rous sarcoma virus (RSV), cytomegalovirus (CMV), the long terminal repeats (LTR) of Moloney murine leukemia virus and other retroviruses, and the thymidine kinase (TK) promoter of herpes simplex virus. Other constitutive promoters are known to those of ordinary skill in the art. The promoters useful as gene expression sequences of the invention also include inducible promoters. Inducible promoters are expressed in the presence of an inducing agent. For example, the metallothionein (MT) promoter is induced to promote transcription and translation in the presence of certain metal ions. Other inducible promoters are known to those of ordinary skill in the art.

10

15

20

25

30

In general, the gene expression sequence shall include, as necessary, 5' non-transcribing and 5' non-translating sequences involved with the initiation of transcription and translation, respectively, such as a TATA box, capping sequence, CAAT sequence, and the like. Especially, such 5' non-transcribing sequences will include a promoter region which includes a promoter sequence for transcriptional control of the operably joined nucleic acid coding sequence for a TLR9 polypeptide. The gene expression sequences optionally include enhancer sequences or upstream activator sequences as desired.

Generally a nucleic acid coding sequence and a gene expression sequence are said to be "operably linked" when they are covalently linked in such a way as to place the transcription and/or translation of the nucleic acid coding sequence under the influence or control of the gene expression sequence. Thus the TLR9 nucleic acid coding sequence and the gene expression sequence are said to be "operably linked" when they are covalently linked in such a way as to place the transcription and/or translation of the TLR9 nucleic acid coding sequence under the influence or control of the gene expression sequence. If it is desired that the TLR9 sequence be translated into a functional protein, two DNA sequences are said to be operably linked if induction of a promoter in the 5' gene expression sequence results in the transcription of the TLR9 sequence and if the nature of the linkage between the two DNA sequences does not (1) result in the introduction of a frame-shift mutation, (2) interfere with the ability of the promoter region to direct the transcription of the TLR9 sequence, or (3) interfere with the ability of the corresponding RNA transcript to be translated into a protein. Thus, a gene expression sequence would be operably linked to a TLR9 nucleic acid sequence if the gene expression sequence were capable of effecting transcription of that TLR9 nucleic acid sequence such that the resulting transcript might be translated into the desired TLR9 protein or polypeptide.

5

10

15

20

25

A "TLR9 ligand" as used herein refers to a molecule that specifically binds a TLR9 polypeptide. In one embodiment the TLR9 ligand specifically binds a TLR9 polypeptide corresponding to at least a ligand-binding portion of the extracellular domain of TLR9. In most instances a TLR9 ligand will also induce TLR9 signaling when contacted with TLR9 under suitable conditions. TLR9 signaling refers to TLR/IL-1R signal transduction mediated through the TLR9, as described in further detail elsewhere herein. As mentioned above, CpG nucleic acids have been reported to be TLR9 ligands, but TLR9 ligands may include other entities as well, including, for example, small molecules. As also previously mentioned, there appears to be a species-specific preference for at least certain TLR9s and certain CpG motifs. As used herein, a species-preferred CpG DNA refers to a particular CpG DNA that is optimized for signal induction by a TLR9 of a particular species. A CpG DNA that is optimized for signal induction by a TLR9 of a particular species refers to a CpG DNA having a sequence that preferentially binds to and/or induces signaling by TLR9 of that species. For example, a human-preferred CpG DNA shall refer to a CpG DNA that optimally stimulates human TLR9 to signal through its TIR domain. Likewise, a murine-preferred CpG DNA

shall refer to a CpG DNA that optimally stimulates murine TLR9 to signal through its TIR domain. Examples of human-preferred and murine-preferred CpG DNA are ODN 2006 (SEO ID NO:58) and 1668 (SEQ ID NO:60), respectively.

The binding and species specificity of TLR9s are believed to be influenced by key amino acids present in the extracellular domain of TLR9. Key amino acids in a TLR9 as used herein refer to those amino acids which contribute significantly to ligand binding and ligand specificity of a particular TLR9 polypeptide.

5

10

15

20

25

A "CpG nucleic acid" or a "CpG immunostimulatory nucleic acid" as used herein is a nucleic acid containing at least one unmethylated CpG dinucleotide (cytosine-guanine dinucleotide sequence, i.e., "CpG DNA" or DNA containing a 5' cytosine followed by 3' guanine and linked by a phosphate bond) which activates a component of the immune system. The entire CpG nucleic acid can be unmethylated or portions may be unmethylated but at least the C of the 5' CG 3' must be unmethylated.

In one embodiment a CpG nucleic acid is represented by at least the formula: 5'-N₁X₁CGX₂N₂-3'

wherein X_1 and X_2 are nucleotides, N is any nucleotide, and N_1 and N_2 are nucleic acid sequences composed of from about 0-25 N's each. In some embodiments X_1 is adenine, guanine, or thymine and/or X_2 is cytosine, adenine, or thymine. In other embodiments X_1 is cytosine and/or X_2 is guanine.

,

Nucleic acids having modified backbones, such as phosphorothioate backbones, also fall within the class of immunostimulatory nucleic acids. U.S. Pat. Nos. 5,723,335 and 5,663,153 issued to Hutcherson, et al. and related PCT publication WO95/26204 describe immune stimulation using phosphorothioate oligonucleotide analogues. These patents describe the ability of the phosphorothioate backbone to stimulate an immune response in a non-sequence specific manner.

An immunostimulatory nucleic acid molecule, including for example a CpG DNA, may be double-stranded or single-stranded. Generally, double-stranded molecules may be more stable *in vivo*, while single-stranded molecules may have increased activity. The terms "nucleic acid" and "oligonucleotide" refer to multiple nucleotides (i.e., molecules comprising a sugar (e.g., ribose or deoxyribose) linked to a phosphate group and to an exchangeable organic base, which is either a substituted pyrimidine (e.g., cytosine (C), thymine (T) or uracil (U)) or a substituted purine (e.g., adenine (A) or guanine (G)) or a modified base. As

used herein, the terms "nucleic acid" and "oligonucleotide" refer to oligoribonucleotides as well as oligodeoxyribonucleotides. The terms shall also include polynucleosides (i.e., a polynucleotide minus the phosphate) and any other organic base-containing polymer. The terms "nucleic acid" and "oligonucleotide" also encompass nucleic acids or oligonucleotides with a covalently modified base and/or sugar. For example, they include nucleic acids having backbone sugars which are covalently attached to low molecular weight organic groups other than a hydroxyl group at the 2' position and other than a phosphate group at the 5' position. Thus modified nucleic acids may include a 2'-O-alkylated ribose group. In addition, modified nucleic acids may include sugars such as arabinose instead of ribose. Thus the nucleic acids may be heterogeneous in backbone composition thereby containing any possible combination of polymer units linked together such as peptide-nucleic acids (which have amino acid backbone with nucleic acid bases). In some embodiments the nucleic acids are homogeneous in backbone composition.

5

10

15

20

25

30

The substituted purines and pyrimidines of the immunostimulatory nucleic acids include standard purines and pyrimidines such as cytosine as well as base analogs such as C-5 propyne substituted bases. Wagner RW et al. (1996) *Nat Biotechnol* 14:840-4. Purines and pyrimidines include but are not limited to adenine, cytosine, guanine, thymine, 5-methylcytosine, 2-aminopurine, 2-amino-6-chloropurine, 2,6-diaminopurine, hypoxanthine, and other naturally and non-naturally occurring nucleobases, substituted and unsubstituted aromatic moieties.

The immunostimulatory nucleic acid is a linked polymer of bases or nucleotides. As used herein with respect to linked units of a nucleic acid, "linked" or "linkage" means two entities are bound to one another by any physicochemical means. Any linkage known to those of ordinary skill in the art, covalent or non-covalent, is embraced. Such linkages are well known to those of ordinary skill in the art. Natural linkages, which are those ordinarily found in nature connecting the individual units of a nucleic acid, are most common. The individual units of a nucleic acid may be linked, however, by synthetic or modified linkages.

Whenever a nucleic acid is represented by a sequence of letters it will be understood that the nucleotides are in 5' to 3' (or equivalent) order from left to right and that "A" denotes adenine, "C" denotes cytosine, "G" denotes guanine, "T" denotes thymidine, and "U" denotes uracil unless otherwise noted.

Immunostimulatory nucleic acid molecules useful according to the invention can be obtained from natural nucleic acid sources (e.g., genomic nuclear or mitochondrial DNA or cDNA), or are synthetic (e.g., produced by oligonucleotide synthesis). Nucleic acids isolated from existing nucleic acid sources are referred to herein as native, natural, or isolated nucleic acids. The nucleic acids useful according to the invention may be isolated from any source, including eukaryotic sources, prokaryotic sources, nuclear DNA, mitochondrial DNA, etc. Thus, the term nucleic acid encompasses both synthetic and isolated nucleic acids.

The immunostimulatory nucleic acids can be produced on a large scale in plasmids, (see *Molecular Cloning: A Laboratory Manual*, J. Sambrook, et al., eds., Second Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, 1989) and separated into smaller pieces or administered whole. After being administered to a subject the plasmid can be degraded into oligonucleotides. One skilled in the art can purify viral, bacterial, eukaryotic, etc. nucleic acids using standard techniques, such as those employing restriction enzymes, exonucleases or endonucleases.

10

15

20

25

30

For use in the instant invention, the immunostimulatory nucleic acids can be synthesized *de novo* using any of a number of procedures well known in the art. For example, the β-cyanoethyl phosphoramidite method (Beaucage SL and Caruthers MH, *Tetrahedron Let* 22:1859 (1981)); nucleoside H-phosphonate method (Garegg et al., *Tetrahedron Let* 27:4051-4054 (1986); Froehler et al., *Nucl Acid Res* 14:5399-5407 (1986); Garegg et al., *Tetrahedron Let* 27:4055-4058 (1986); Gaffney et al., *Tetrahedron Let* 29:2619-2622 (1988)). These chemistries can be performed by a variety of automated oligonucleotide synthesizers available in the market.

The immunostimulatory nucleic acid may be any size of at least 6 nucleotides but in some embodiments are in the range of between 6 and 100 or in some embodiments between 8 and 35 nucleotides in size. Immunostimulatory nucleic acids can be produced on a large scale in plasmids. These may be administered in plasmid form or alternatively they can be degraded into oligonucleotides before administration.

A "stabilized immunostimulatory nucleic acid" shall mean a nucleic acid molecule that is relatively resistant to *in vivo* degradation (e.g., via an exo- or endo-nuclease). Stabilization can be a function of length or secondary structure. Nucleic acids that are tens to hundreds of kbs long are relatively resistant to *in vivo* degradation. For shorter nucleic acids, secondary structure can stabilize and increase their effect. For example, if the 3' end of an

5

10

15

20

25

30

oligonucleotide has self-complementarity to an upstream region, so that it can fold back and form a sort of stem loop structure, then the oligonucleotide becomes stabilized and therefore exhibits more activity.

Some stabilized immunostimulatory nucleic acids have a modified backbone. It has been demonstrated that modification of the oligonucleotide backbone provides enhanced activity of the immunostimulatory nucleic acids when administered *in vivo*. Nucleic acids, including at least two phosphorothioate linkages at the 5' end of the oligonucleotide and multiple phosphorothioate linkages at the 3' end, preferably 5, may provide maximal activity and protect the oligonucleotide from degradation by intracellular exo- and endo-nucleases. Other modified oligonucleotides include phosphodiester modified oligonucleotide, combinations of phosphodiester and phosphorothioate oligonucleotide, methylphosphonate, methylphosphorothioate, phosphorodithioate, and combinations thereof. Each of these combinations and their particular effects on immune cells is discussed in more detail in U.S. Pat. Nos. 6,194,388 and 6,207,646, the entire contents of which are incorporated herein by reference. It is believed that these modified oligonucleotides may show more stimulatory activity due to enhanced nuclease resistance, increased cellular uptake, increased protein binding, and/or altered intracellular localization. Both phosphorothioate and phosphodiester nucleic acids are active in immune cells.

Other stabilized immunostimulatory nucleic acids include: nonionic DNA analogs, such as alkyl- and aryl-phosphates (in which the charged phosphonate oxygen is replaced by an alkyl or aryl group), phosphodiester and alkylphosphotriesters, in which the charged oxygen moiety is alkylated. Oligonucleotides which contain diol, such as tetraethyleneglycol or hexaethyleneglycol, at either or both termini have also been shown to be substantially resistant to nuclease degradation.

Phosphorothioate nucleic acid molecules may be synthesized using automated techniques employing either phosphoramidate or H-phosphonate chemistries. Aryl- and alkyl-phosphonates can be made, e.g., as described in U.S. Pat. No. 4,469,863; and alkylphosphotriesters (in which the charged oxygen moiety is alkylated as described in U.S. Pat. No. 5,023,243 and European Patent No. 092,574) can be prepared by automated solid phase synthesis using commercially available reagents. Methods for making other DNA backbone modifications and substitutions have been described. Uhlmann E and Peyman A (1990) Chem Rev 90:544; Goodchild J (1990) Bioconjugate Chem 1:165.

10

15

20

25

30

Other sources of immunostimulatory nucleic acids useful according to the invention include standard viral and bacterial vectors, many of which are commercially available. In its broadest sense, a "vector" is any nucleic acid material which is ordinarily used to deliver and facilitate the transfer of nucleic acids to cells. The vector as used herein may be an empty vector or a vector carrying a gene which can be expressed. In the case when the vector is carrying a gene the vector generally transports the gene to the target cells with reduced degradation relative to the extent of degradation that would result in the absence of the vector. In this case the vector optionally includes gene expression sequences to enhance expression of the gene in target cells such as immune cells, but it is not required that the gene be expressed in the cell.

Nucleic acid-binding fragments of TLRs are believed to include the extracytoplasmic (extracellular) domain or subportions thereof, such as those which include at least an MBD motif, a CXXC motif, or both an MBD motif and a CXXC motif.

Both mouse and human TLR9 have an N-terminal extension of approximately 180 amino acids compared to other TLRs. An insertion also occurs at amino acids 253-268, which is not found in TLRs 1-6 but is present in human TLR7 and human TLR8. This insert has two CXXC motifs which participate in forming a CXXC domain. The CXXC domain resembles a zinc finger motif and is found in DNA-binding proteins and in certain specific CpG binding proteins, e.g., methyl-CpG binding protein-1 (MBD-1). Fujita N et al. (2000) *Mol Cell Biol* 20:5107-18. Both human and mouse TLR9 CXXC domains occur at aa 253-268:

CXXC motif:	GNCXXCXXXXXCXXC	SEQ ID NO:62
Human TLR9:	GNCRRCDHAPNPCMEC	SEQ ID NO:63
Murine TLR9:	GNCRRCDHAPNPCMIC	SEQ ID NO:64

An additional motif believed to be involved in CpG binding is the MBD motif, also found in MBD-1, listed below as SEQ ID NO:53. Fujita, N et al.(2000) *Mol Cell Biol* 20:5107-18; Ohki I et al. (1999) *EMBO J* 18:6653-61. Amino acids 524-554 of hTLR9 and aa 525-555 of mTLR9 correspond to the MBD motif of MBD-1 as shown:

MBD motif:

WO 2004/026888

5

10

15

20

25

30

PCT/US2003/029577

MBD-1	R-XXXXXXX-R-X-D-X-Y-XXXXXXXXX-R-S-XXXXXXX-Y	SEQ ID NO:65
hTLR9	Q-XXXXXXX-K-X-D-X-Y-XXXXXXXXX-R-L-XXXXXXX-Y	SEQ ID NO:66
mTLR9	O-XXXXXX-K-X-D-X-A-XXXXXXXXX-O-P-XXXXXXX-A	SEQ ID NO:67
hTLR9	Q-VLDLSRN-K-L-D-L-Y-HEHSFTELP-R-L-EALDLS-Y	SEQ ID NO:68
mTLR9	O-VLDLSHN-K-L-D-L-Y-HWKSFSELP-O-L-OALDLS-Y	SEO ID NO:69

- 36 -

Although the signaling functions of MBD-1 and TLR9 are quite different, the core D-X-Y is conserved and is believed to be involved in CpG binding.

According to another aspect of the invention, a screening method is provided for identifying an immunostimulatory compound. The method according to this aspect of the invention involves contacting a functional TLR9 with a test compound; detecting presence or absence of a response mediated by a TLR9 signal transduction pathway in the presence of the test compound arising as a result of an interaction between the functional TLR9 and the test compound; and determining the test compound is an immunostimulatory compound when the presence of a response mediated by the TLR9 signal transduction pathway is detected.

An immunostimulatory compound is a natural or synthetic compound that is capable of inducing an immune response when contacted with an immune cell. A TLR9 ligand that is an immunostimulatory compound is a natural or synthetic compound that is capable of inducing an immune response when contacted with an immune cell that expresses TLR9. A TLR9 ligand that is an immunostimulatory compound is also a natural or synthetic compound that is capable of inducing a TLR/IL-1R signal transduction pathway when contacted with a TLR9. Immunostimulatory compounds include but are not limited to immunostimulatory nucleic acids. The immunostimulatory compound can be, for example, a nucleic acid molecule, polynucleotide or oligonucleotide, a polypeptide or oligopeptide, a lipid or lipopolysaccharide, a small molecule.

A basis for certain of the screening assays is the presence of a functional TLR9 in a cell. The functional TLR9 in some instances is naturally expressed by a cell. In other instances, expression of the functional TLR9 can involve introduction or reconstitution of a species-specific TLR9 into a cell or cell line that otherwise lacks the TLR9 or lacks responsiveness to immunostimulatory nucleic acid, resulting in a cell or cell line capable of activating the TLR/IL-1R signaling pathway in response to contact with an

135

10

15

20

25

30

immunostimulatory nucleic acid. In yet other instances, expression of the functional TLR9 can involve introduction of a chimeric or modified TLR9 into a cell or cell line that otherwise lacks the TLR9 or lacks responsiveness to immunostimulatory nucleic acid, resulting in a cell or cell line capable of activating the TLR/IL-1R signaling pathway in response to contact with an immunostimulatory nucleic acid. Examples of cell lines lacking TLR9 or immunostimulatory nucleic acid responsiveness include, but are not limited to, 293 fibroblasts (ATCC CRL-1573), MonoMac-6, THP-1, U937, CHO, and any TLR9 knock-out. The introduction of the species-specific, chimeric or modified TLR9 into the cell or cell line is preferably accomplished by transient or stable transfection of the cell or cell line with a TLR9-encoding nucleic acid sequence operatively linked to a gene expression sequence (as described above). Methods for transient and for stable transfection of a cell are well known in the art.

The screening assays can have any of a number of possible readout systems based upon either TLR/IL-1R signaling pathway or other assays useful for assessing response to immunostimulatory nucleic acids. It has been reported that immune cell activation by CpG immunostimulatory sequences is dependent in some way on endosomal processing.

In certain embodiments, the readout for the screening assay is based on the use of native genes or, alternatively, cotransfected or otherwise co-introduced reporter gene constructs which are responsive to the TLR/IL-1R signal transduction pathway involving MyD88, TRAF, p38, and/or ERK. Häcker H et al. (1999) *EMBO J* 18:6973-6982. These pathways activate kinases including κB kinase complex and c-Jun N-terminal kinases. Thus reporter genes and reporter gene constructs particularly useful for the assays can include a reporter gene operatively linked to a promoter sensitive to NF-κB. Examples of such promoters include, without limitation, those for NF-κB, IL-1β, IL-6, IL-8, IL-12 p40, CD80, CD86, and TNF-α. The reporter gene operatively linked to the TLR-sensitive promoter can include, without limitation, an enzyme (e.g., luciferase, alkaline phosphatase, β-galactosidase, chloramphenicol acetyltransferase (CAT), etc.), a bioluminescence marker (e.g., greenfluorescent protein (GFP, U.S. Pat. No. 5,491,084), blue fluorescent protein, etc.), a surface-expressed molecule (e.g., CD25), and a secreted molecule (e.g., IL-8, IL-12 p40, TNF-α). In certain embodiments the reporter is selected from IL-8, TNF-α, NF-κB-luciferase (NF-κB-luc; Häcker H et al. (1999) *EMBO J* 18:6973-6982), IL-12 p40-luc (Murphy TL et al. (1995)

Mol Cell Biol 15:5258-5267), and TNF-luc (Häcker H et al. (1999) EMBO J 18:6973-6982). At least one of these reporter constructs (NF-κB-luc) is commercially available (Stratagene, La Jolla, CA). In assays relying on enzyme activity readout, substrate can be supplied as part of the assay, and detection can involve measurement of chemiluminescence, fluorescence, color development, incorporation of radioactive label, drug resistance, or other marker of enzyme activity. For assays relying on surface expression of a molecule, detection can be accomplished using FACS analysis or functional assays. Secreted molecules can be assayed using enzyme-linked immunosorbent assay (ELISA) or bioassays. Many such readout systems are well known in the art and are commercially available.

According to one embodiment of this method, comparison can be made to a reference immunostimulatory nucleic acid. The reference immunostimulatory nucleic acid may be any suitably selected immunostimulatory nucleic acid, including a CpG nucleic acid. In certain embodiments the screening method is performed using a plurality of test nucleic acids. In certain embodiments comparison of test and reference responses is based on comparison of quantitative measurements of responses in each instance.

10

15

20

25

30

In another aspect the invention provides a screening method for identifying species specificity of an immunostimulatory nucleic acid. The method involves contacting a TLR9 of a first species with a test immunostimulatory nucleic acid; contacting a TLR9 of a second species with the test immunostimulatory nucleic acid; measuring a response mediated by a TLR signal transduction pathway associated with the contacting the TLR9 of the first species with the test immunostimulatory nucleic acid; measuring a response mediated by the TLR signal transduction pathway associated with the contacting the TLR9 of the second species with the test immunostimulatory nucleic acid; and comparing the two responses. The TLR9 may be expressed by a cell or it may be part of a cell-free system. The TLR9 may be part of a complex, with either another TLR or with another protein, e.g., MyD88, IRAK, TRAF, IkB, NF-kB, or functional homologues and derivatives thereof. Thus for example a given ODN can be tested against a panel of human fibroblast 293 fibroblast cells transfected with TLR9 from various species and optionally cotransfected with a reporter construct sensitive to TLR/IL-1R activation pathways. Thus in another aspect, the invention provides a method for screening species selectivity with respect to a given nucleic acid sequence.

Test compounds can include but are not limited to peptide nucleic acids (PNAs), antibodies, polypeptides, carbohydrates, lipids, hormones, and small molecules. Test

compounds can further include variants of a reference immunostimulatory nucleic acid incorporating any one or combination of the substitutions described above. Test compounds can be generated as members of a combinatorial library of compounds.

5

10

15

20

30

In preferred embodiments, the screening methods can be performed on a large scale and with high throughput by incorporating, e.g., an array-based assay system and at least one automated or semi-automated step. For example, the assays can be set up using multiple-well plates in which cells are dispensed in individual wells and reagents are added in a systematic manner using a multiwell delivery devices suited to the geometry of the multiwell plate.

Manual and robotic multiwell delivery devices suitable for use in a high throughput screening assay are well known by those skilled in the art. Each well or array element can be mapped in a one-to-one manner to a particular test condition, such as the test compound. Readouts can also be performed in this multiwell array, preferably using a multiwell plate reader device or the like. Examples of such devices are well known in the art and are available through commercial sources. Sample and reagent handling can be automated to further enhance the throughput capacity of the screening assay, such that dozens, hundreds, thousands, or even millions of parallel assays can be performed in a day or in a week. Fully robotic systems are known in the art for applications such as generation and analysis of combinatorial libraries of synthetic compounds. See, for example, U.S. Pat. Nos. 5,443,791 and 5,708,158.

The following examples are provided for illustrative purposes and are not meant to be limiting in any way.

Examples

25 Example 1. Cloning and Sequencing of Rat, Porcine, Bovine, Equine, Ovine, Canine, and Feline TLR9

Cells and Tissues. Lymphoid tissues, primarily spleen or blood mononuclear cells (PBMC) from five mammalian species were collected: mouse, pig, bovine, rat and horse. Spleen samples were collected in RNAlaterTM (Ambion[®], Austin, TX, USA), stabilized at 4°C overnight and stored at -70°C. Blood samples were centrifuged at 500 x g for 25 min at room temperature and the buffy coat, containing enriched PBMC, was then removed and stored at -70°C. The mouse specimen was used as a comparative positive control.

First-strand cDNA synthesis. Total RNA from the spleen and PBMC samples was isolated using a monophasic solution of phenol and guanidine isothiocyanate: TRIzolTM reagent (GIBCO BRL[®], Burlington, ON, Canada) according to the manufacturer's instructions. First-strand cDNA was synthesized from the total RNA using SUPERSCRIPTTM II reverse transcriptase (GIBCO BRL[®], Burlington, ON, Canada). Approximately 3 μg of total RNA was added to 50 pmoles of oligo(dT) primer [poly T₍₁₈₎]; the mixture was heated to 70°C for 10 min and subsequently chilled on ice. The following was added to the cooled reaction mixture: 1 μl of mixed dNTP stock containing 10 mM each dATP, dCTP, dGTP and dTTP (Amersham Pharmacia Biotech Inc., Baie de Urfe, Quebec) at neutral pH, 1X first strand buffer (50 mM Tris-HCl pH 8.3/ 75 mM KCl/ 3 mM MgCl₂) and 2 μl of 0.1 M DTT. The mixture was subsequently heated to 42°C for 2 min, followed by addition of 200 units of SUPERSCRIPTTM II reverse transcriptase. The reaction was carried out at 42°C for 50 min, followed by 70°C for 15 min. The first-strand cDNA was used as the template for subsequent polymerase chain reaction (PCR) amplifications.

10

15

20

25

30

mentioned species using primers designed from known mouse and human TLR9 sequence in Genbank: Accession AF314224 and AF259262, respectively. The primers were designed using the primer design software, Clone Manager 5 (Scientific and Educational Software, Durham, NC, USA). TLR9 gene-specific primers used were: forward primer 5'-ACCTTGCCTGCCTTCCTACCCTGTGA-3' (SEQ ID NO:37) and reverse primer 5'-GTCCGTGTGGGCCAGCACAAA-3' (SEQ ID NO:38). The 2.7 Kbp fragment was PCR amplified using Advantage® 2 DNA polymerase mix (BD Biosciences Clontech, Palo Alto, CA, USA) according to the manufacturer's instructions. PCR reaction volumes of 25 µl contained 15 pmoles of each primer, 0.2 mM of dNTP mix and 1 µl of reverse transcription reaction. PCR amplification was conducted by initial denaturation at 94°C for 1 min followed by 30 cycles of 94°C denaturation (15 sec), 65°C annealing (45 sec) and 72°C extensions (2 min), with a final extension at 72°C for 5 min.

PCR amplification. TLR9 gene was PCR amplified from each of the above-

Cloning and sequencing. The PCR amplified fragment was treated with 500 units of T4 DNA polymerase (Amersham Pharmacia Biotech Inc., Baie de Urfe, Quebec) for 15 min at room temperature prior to cleaning the reaction with QIAquick PCR purification kit (QIAGEN Inc., Mississauga, ON, Canada). The fragment was then ligated to pZErOTM - 2

- 41 -

vector (Invitrogen[™] Life Technologies, Burlington, ON, Canada), treated with *Eco RV* restriction enzyme, using T4 DNA Ligase (GIBCO BRL[®], Burlington, ON, Canada). *E. coli* TOP 10 chemically competent cells (Invitrogen[™] Life Technologies, Burlington, ON, Canada) were used to transform ligated products. Plasmids containing the 2.7 Kbp fragment were sequenced using an automated DNA sequencer, CEQ[™] 2000XL DNA analysis system (Beckman Coulter Inc., Fullerton, CA, USA).

Sequences of the 2.7 Kbp fragment were derived from three clones of each species selected from independent PCR reactions to account for errors that may have been incurred during the PCR amplifications and to confirm the sequence data.

Nucleotide sequences of the rat, porcine, bovine, equine, ovine, canine, and feline TLR9 were extended and completed using standard 5' and 3' RACE PCR and primers designed using the sequences obtained from the 2.7 Kbp fragments.

10

15

20

25

30

Results. Nucleotide sequences of rat, porcine, bovine, equine, canine, and feline TLR9 cDNA obtained by the methods above are provided as SEQ ID NOs 3, 7, 11, 15, 19, 23, and 27, respectively. Deduced amino acid sequences are provided as SEQ ID NOs 1, 5, 9, 13, 17, 21, and 25, respectively. Deduced amino acid sequences of full-length murine and human TLR9 are provided as SEQ ID NOs 29 and 33, respectively.

Example 2. Comparison of Aligned Sequences for TLR9 from Various Mammalian Species.

Multiple sequence alignment of deduced amino acid sequences for feline, canine, bovine, mouse, ovine, porcine, horse, human, and rat TLR9 polypeptides was performed using Clustal W 1.82 (see, for example, www.cmbi.kun.nl/bioinf/tools/clustalw.shtml). In addition, paired sequence alignment of deduced amino acid sequences for murine and human TLR9 polypeptides was performed using Clustal W 1.82. The results of the multiple sequence alignment are presented in Figure 1. As will be appreciated from Figure 1, certain amino acids are highly conserved across all species examined. Similarly, certain amino acids differ only by conservative amino acid substitutions among the various species. In addition, it is evident that certain amino acids which are conserved between murine and human TLR9 are not conserved in other species. Furthermore, Figure 1 also indicates that certain amino acids are highly divergent across various species. The information provided by the comparison of multiple species adds significantly to the information available by comparison between only murine and human TLR9 sequences.

The putative transmembrane regions of the TLR9 polypeptides are indicated in boxes in Figure 1. Sequence upstream of each transmembrane region is extracellular domain and is believed to include sequence primarily responsible for binding to TLR9 ligands, including CpG DNA. The extracellular domains of feline, canine, bovine, mouse, ovine, porcine, horse, human, and rat TLR9 correspond to amino acids numbered 1-820, 1-822, 1-818, 1-821, 1-818, 1-819, 1-820, 1-820, and 1-821, respectively, as shown in Figure 1.

Figure 2 presents an evolutionary relatedness tree for six TLR9 polypeptides examined. The cladogram in Figure 2 was prepared using Clustal W (see above). As can be appreciated from this figure, murine and human TLR9 are nearly the most divergent TLR9s in this group. Surprisingly, human and horse TLR9 appear relatively closely related.

Example 3. Reconstitution of TLR9 Signaling in 293 Fibroblasts.

10

15

20

25

30

Mouse TLR9 cDNA (SEQ ID NO:31) and human TLR9 cDNA (SEQ ID NO:35) in pT-Adv vector (from Clonetech) were individually cloned into the expression vector pcDNA3.1(-) from Invitrogen using the EcoRI site. Utilizing a "gain of function" assay it was possible to reconstitute human TLR9 (hTLR9) and murine TLR9 (mTLR9) signaling in CpG-DNA non-responsive human 293 fibroblasts (ATCC, CRL-1573). The expression vectors mentioned above were transfected into 293 fibroblast cells using the calcium phosphate method.

Since NF-κB activation is central to the IL-1/TLR signal transduction pathway (Medzhitov R et al. (1998) *Mol Cell* 2:253-258; Muzio M et al. (1998) *J Exp Med* 187:2097-101), cells were transfected with hTLR9 or co-transfected with hTLR9 and an NF-κB-driven luciferase reporter construct. Human fibroblast 293 cells were transiently transfected with hTLR9 and a six-times NF-κB-luciferase reporter plasmid (NF-κB-luc) or with hTLR9 alone. After stimulus with CpG-ODN (2006, 2μM, TCGTCGTTTTGTCGTTTTGTCGTT, SEQ ID NO:58), GpC-ODN (2006-GC, 2μM, TGCTGCTTTTGTGCTTTTGTGCTT, SEQ ID NO:59), LPS (100 ng/ml) or media, NF-κB activation by luciferase readout (8h) or IL-8 production by ELISA (48h) were monitored. Results representative of three independent experiments showed that cells expressing hTLR9 responded to CpG-DNA but not to LPS.

Independently, human fibroblast 293 cells were transiently transfected with mTLR9 and the NF-κB-luc construct or with mTLR9 alone. After stimulation with CpG-ODN (1668, 2μM; TCCATGACGTTCCTGATGCT, SEQ ID NO:60), GpC-ODN (1668-GC, 2μM;

TCCATGAGCTTCCTGATGCT, SEQ ID NO:61), LPS (100 ng/ml) or media, NF-κB activation by luciferase readout (8h) or IL-8 production by ELISA (48h) were monitored. Results showed that expression of TLR9 (human or mouse) in 293 cells results in a gain of function for CpG-DNA stimulation.

To generate stable clones expressing human TLR9, murine TLR9, or either TLR9 with the NF-κB-luc reporter plasmid, 293 cells were transfected in 10 cm plates (2x10⁶ cells/plate) with 16 μg of DNA and selected with 0.7 mg/ml G418 (PAA Laboratories GmbH, Cölbe, Germany). Clones were tested for TLR9 expression by RT-PCR. The clones were also screened for IL-8 production or NF-κB-luciferase activity after stimulation with ODN. Four different types of clones were generated.

293-hTLR9-luc:

expressing human TLR9 and 6-fold NF-kB-luciferase reporter

293-mTLR9-luc:

expressing murine TLR9 and 6-fold NF-kB-luciferase reporter

293-hTLR9:

expressing human TLR9

15 293-mTLR9:

5

10

20

25

expressing murine TLR9

Results indicated that stable clones also responded to CpG-ODN.

Example 4. Similar ODN Sequence Specificity of TLR9 of Human and Equine TLR9.

 $3x10^6$ 293T cells were electroporated with $5\mu g$ NF- κB -luc plasmid and $5\mu g$ of either horse TLR9-pcDNA3.1 plasmid or humanTLR9-pcDNA3.1 plasmid at 200V, 975 μF . After the electroporation the cells were plated in 96-well cell culture plates at $2.5x10^4$ cells per well and grown overnight at 37°C. The cells were stimulated with the indicated concentration of ODN for 16h, after which the supernatant was removed and the cells lysed in lysis buffer and frozen for at least 2 hours at $-80^{\circ}C$. Luciferase activity was measured by adding Luciferase Assay substrate from Promega. Values are given as fold specific induction over non-stimulated control. Results are shown in **Figure 3**.

As shown in Figure 3, ODN 2006 (TCGTCGTTTTGTCGTTTTGTCGTT; SEQ ID NO:58) has a strong specificity for human TLR9. ODN 1982

(TCCAGGACTTCTCAGGTT; SEQ ID NO:70) was the negative control ODN. ODN5890 (TCCATGACGTTTTTGATGTT; SEQ ID NO:39) has a strong specificity for mouse

- 44 -

TLR9. This experiment demonstrates the similarity of horse TLR9 to human TLR9 in binding specificity, a result predicted by the evolutionary relatedness of horse TLR9 to human TLR9. Mouse TLR9 is more distant from horse TLR9 and human TLR9 in sequence homology, and ODN 5890 was not detected by either human or horse TLR9.

5

10

Example 5. Non-human, Non-murine Native Mammalian TLR9 Useful in Screening for Human-Preferred CpG DNA.

Native rat, porcine, bovine, equine, and ovine TLR9 polypeptides are screened for binding or TLR9 signaling activity when contacted with human-preferred CpG DNA (ODN 2006). Rat, porcine, bovine, equine, or ovine TLR9 polypeptides which exhibit significant TLR9 binding or TLR9 signaling activity in this assay are then used as the basis for screening for additional human-preferred CpG DNA. An expression vector containing a nucleic acid sequence encoding a selected native rat, porcine, bovine, equine, or ovine TLR9 polypeptide, and optionally a reporter construct, is introduced into cells which do not express TLR9. The cells expressing the selected native rat, porcine, bovine, equine, or ovine TLR9 polypeptide are contacted with candidate human-preferred CpG DNA. Candidate human-preferred CpG DNA exhibiting significant TLR9 binding or TLR9 signaling activity are selected as human-preferred CpG DNA.

20 E

Example 6. Chimeric TLR9 Useful in Screening for Human-Preferred CpG DNA.

Chimeric TLR9 polypeptides are screened for binding or TLR9 signaling activity when contacted with human-preferred CpG DNA (ODN 2006). Chimeric TLR9 polypeptides which exhibit significant TLR9 binding or TLR9 signaling activity in this assay are then used as the basis for screening for additional human-preferred CpG DNA. An expression vector containing a nucleic acid sequence encoding a selected chimeric TLR9 polypeptide, and optionally a reporter construct, is introduced into cells which do not express TLR9. The cells expressing the selected chimeric TLR9 polypeptide are contacted with candidate human-preferred CpG DNA. Candidate human-preferred CpG DNA exhibiting significant TLR9 binding or TLR9 signaling activity are selected as human-preferred CpG DNA.

30

25

Example 7. Chimeric TLR9 Responsive to Both Human-Preferred and Murine-Preferred CpG DNA.

- 45 -

Chimeric TLR9 polypeptides are screened for binding or TLR9 signaling activity when contacted with human-preferred CpG DNA (ODN 2006) and also screened for binding or TLR9 signaling activity when contacted with murine-preferred CpG DNA (ODN 1668). Chimeric TLR9 polypeptides which exhibit significant TLR9 binding or TLR9 signaling activity in each of these assays are then used as the basis for screening for additional human-preferred CpG DNA and for screening for additional murine-preferred CpG DNA. An expression vector containing a nucleic acid sequence encoding a selected chimeric TLR9 polypeptide, and optionally a reporter construct, is introduced into cells which do not express TLR9. The cells expressing the selected chimeric TLR9 polypeptide are contacted with candidate human-preferred CpG DNA or candidate murine-preferred CpG DNA. Candidate human-preferred CpG DNA exhibiting significant TLR9 binding or TLR9 signaling activity are selected as human-preferred CpG DNA. Candidate murine-preferred CpG DNA exhibiting significant TLR9 binding or TLR9 signaling activity are selected as murine-preferred CpG DNA.

15

20

10

5

Equivalents

The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by examples provided, since the examples are intended as a single illustration of one aspect of the invention and other functionally equivalent embodiments are within the scope of the invention. Various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims. The advantages of the invention are not necessarily encompassed by each embodiment of the invention.

25 :...

All references, patents and patent publications that are recited in this application are incorporated in their entirety herein by reference.

We claim:

5

15

20

25

30

Claims

- 1. An isolated polypeptide comprising an amino acid sequence selected from the group SEQ ID NO:1, SEQ ID NO:5, SEQ ID NO:9, SEQ ID NO:13, and SEQ ID NO:17.
- 2. An isolated polypeptide comprising an amino acid sequence selected from the group SEQ ID NO:2, SEQ ID NO:6, SEQ ID NO:10, SEQ ID NO:14, and SEQ ID NO:18.
- An isolated nucleic acid molecule comprising a nucleic acid sequence encoding a
 polypeptide comprising an amino acid sequence selected from the group SEQ ID NO:1, SEQ
 ID NO:5, SEQ ID NO:9, SEQ ID NO:13, and SEQ ID NO:17.
 - 4. An isolated nucleic acid molecule comprising a nucleic acid sequence encoding a polypeptide comprising an amino acid sequence selected from the group SEQ ID NO:2, SEQ ID NO:6, SEQ ID NO:10, SEQ ID NO:14, and SEQ ID NO:18.
 - 5. A vector comprising the nucleic acid of any of claims 3-4.
 - 6. A cell comprising the vector of claim 5.
 - 7. An antibody or fragment thereof that binds specifically to the polypeptide of any of claims 1-2.
 - 8. A method for identifying key amino acids in a TLR9 of a first species which confer specificity for CpG DNA optimized for TLR9 of the first species, comprising:

aligning protein sequences of TLR9 of a first species, TLR9 of a second species, and TLR9 of a third species, wherein the TLR9 of the third species preferentially generates a signal when contacted with a CpG DNA optimized for TLR9 of the first species rather than when contacted with a CpG DNA optimized for TLR9 of the second species;

generating an initial set of candidate amino acids in the TLR9 of the first species by excluding each amino acid in the TLR9 of the first species which (a) is identical with the

- 47 -

TLR9 of the second species or (b) differs from the TLR9 of the second species only by conservative amino acid substitution;

generating a refined set of candidate amino acids by selecting each amino acid in the initial set of candidate amino acids in the TLR9 of the first species which (a) is identical with the TLR9 of the third species or (b) differs from the TLR9 of the third species only by conservative amino acid substitution; and

identifying as key amino acids in the TLR9 of the first species each amino acid in the refined set of candidate amino acids.

9. A method for identifying key amino acids in human TLR9 which confer specificity for CpG DNA optimized for human TLR9, comprising:

aligning protein sequences of human TLR9, murine TLR9, and TLR9 of a third species, wherein the TLR9 of the third species preferentially generates a signal when contacted with a CpG DNA optimized for human TLR9 rather than when contacted with a CpG DNA optimized for murine TLR9;

generating an initial set of candidate amino acids in human TLR9 by excluding each amino acid in human TLR9 which (a) is identical with murine TLR9 or (b) differs from murine TLR9 only by conservative amino acid substitution;

generating a refined set of candidate amino acids by selecting each amino acid in the initial set of candidate amino acids in human TLR9 which (a) is identical with the TLR9 of the third species or (b) differs from the TLR9 of the third species only by conservative amino acid substitution; and

identifying as key amino acids in human TLR9 each amino acid in the refined set of candidate amino acids.

25

30

10

15

20

10. The method according to claim 9, performed iteratively with a plurality of TLR9s derived from different species other than human and mouse, wherein for each TLR9 the refined set of candidate amino acids is assigned a weight, said weight corresponding to a ratio equal to (responsiveness to human-preferred CpG DNA)/(responsiveness to murine-preferred CpG DNA).

- 48 -

- 11. An isolated polypeptide comprising an amino acid sequence identical to SEQ ID NO:30 except for substitution of at least one key amino acid identifed according to the method of any of claims 9 or 10.
- 12. An isolated nucleic acid molecule comprising a nucleic acid sequence encoding a polypeptide according to claim 11.
 - 13. A vector comprising the nucleic acid of claim 12.
- 10 14. A cell comprising the vector of claim 13.
 - 15. An antibody that binds specifically to the polypeptide of claim 14.
 - 16. A screening method to identify a TLR9 ligand, comprising: contacting a polypeptide according to any of claims 1, 2, or 11 with a candidate TLR9 ligand;

measuring a signal in response to the contacting; and identifying the candidate TLR9 ligand as a TLR9 ligand when the signal in response to the contacting is consistent with TLR9 signaling.

20

15

- 17. The method of claim 16, wherein the signal comprises expression of a reporter gene responsive to TLR/IL-1R signal transduction pathway.
- 18. The method of claim 17, wherein the reporter gene is operatively linked to a promoter sensitive to NF-κB.
 - 19. The method of claim 17, wherein the candidate TLR9 ligand is an immunostimulatory nucleic acid.
- 20. The method of claim 19, wherein the immunostimulatory nucleic acid is CpG DNA.

- 49 -

21. A screening method to identify species-specific CpG-motif preference of an isolated polypeptide of claim 2 or claim 11, comprising:

contacting an isolated polypeptide of claim 2 or claim 11 with a CpG DNA comprising a hexamer sequence selected from the group consisting of GACGTT, AACGTT, CACGTT, TACGTT, GGCGTT, GCCGTT, GTCGTT, GATGTT, GAAGTT, GAGGTT, GACATT, GACCTT, GACGTT, G

measuring a signal in response to the contacting; and

identifying a species-specific CpG-motif preference when the signal in response to the contacting is consistent with TLR9 signaling.

- 22. The method of claim 21, wherein the signal comprises expression of a reporter gene responsive to TLR/IL-1R signal transduction pathway.
- 23. The method of claim 17, wherein the reporter gene is operatively linked to a promoter sensitive to NF-κB.
 - 24. The method of claim 21, wherein the CpG DNA is an oligodeoxynucleotide having a sequence selected from the group consisting of

```
TCCATGACGTTTTTGATGTT
                                    (SEQ ID NO:39),
20
                                    (SEQ ID NO:40),
         TCCATAACGTTTTTGATGTT
                                    (SEQ ID NO:41),
         TCCATCACGTTTTTGATGTT
         TCCATTACGTTTTTGATGTT
                                    (SEQ ID NO:42),
         TCCATGGCGTTTTTGATGTT
                                    (SEQ ID NO:43),
                                    (SEQ ID NO:44),
         TCCATGCCGTTTTTGATGTT
25
         TCCATGTCGTTTTTGATGTT
                                    (SEQ ID NO:45),
                                    (SEQ ID NO:46),
         TCCATGATGTTTTTGATGTT
         TCCATGAAGTTTTTGATGTT
                                    (SEQ ID NO:47),
         TCCATGAGGTTTTTGATGTT
                                    (SEQ ID NO:48),
         TCCATGACATTTTTGATGTT
                                    (SEQ ID NO:49),
30
         TCCATGACCTTTTTGATGTT
                                    (SEQ ID NO:50),
         TCCATGACTTTTTTGATGTT
                                    (SEO ID NO:51),
         TCCATGACGCTTTTGATGTT
                                    (SEQ ID NO:52),
         TCCATGACGATTTTGATGTT
                                    (SEQ ID NO:53),
                                     (SEQ ID NO:54),
         TCCATGACGGTTTTGATGTT
35
         TCCATGACGTCTTTGATGTT
                                     (SEQ ID NO:55),
         TCCATGACGTATTTGATGTT
                                     (SEQ ID NO:56), and
                                     (SEO ID NO:57).
         TCCATGACGTGTTTGATGTT
```

Figure 1 (1/3)

PCT/US2003/029577

feline	MGPCHGALHPLSLLVQAAALAVALAQGTLPAFLPCELQRHGLVNCDWLFLKSVPHFSAAA	
canine	MGPCRGALHPLSLLVQAAALALAOGTLPAFLPCELOPHGLVNCNWLFT.KGVDDEGAAA	CO
bovine	MGP-ICAPHPLSLLVQAAALAAALAEGTI.PAFI.PCEI.QPHGQVDCMWI.ET WGVDUEGD.CD	F 0
mouse	MGP-YCAPHPLSLLVQAAALAAALAEGTLPAFLPCELQPHGQVDCNWLFLKSVPHFSAGA	59
ovine	MGP-ICAPHPLSLLVQAAALAAALAOGTLPAFLPCELOPRGKVNCNWI.FLKGVPDFGACA	EΛ
porcine	MGP-RCTLHPLSLLVQVTALAAALAQGRLPAFLPCELQPHGLVNCNWLFLKSVPHFSAAA	59
horse	MGPCHGALQPLSLLVQAAMLAVALAQGTLPPFLPCELQPHGLVNCNWLFLKSVPHFSAAA	59
human	MGFCRSALHPLSLLVQAIMLAMTLALGTLPAFLPCELQPHGLVNCNWLFLKSVPHFSMAA	60
rat	MVLCRRTLHPLSLLVQAAVLAEALALGTLPAFLPCELKPHGLVDCNWLFLKSVPHFSAAE	60
	* ::****** ** :** ******: :* *:*:******	60
feline	PRGNVTSLSLYSNRIHHLHDSDFVHLSSLRRLNLKWNCPPASLSPMHFPCHMTIEPHTFL	
canine	PRGNVTSLSLYSNRIHHLHDYDFVHFVHLRRLNLKWNCPPASLSPMHFPCHMTIEPNTFL	120
bovine	PRANVTSLSLISNRIHHLHDSDFVHLSNLRVLNLKWNCPPAGLSPMHFPCHMTIEPNTFL	120
mouse	PRANVTSLSLISNRIHHLHDSDFVHLSNLRVLNLKWNCPPAGLSPMHFPCRMTIEPNTFL	119
ovine	PRANVTSLSLISNRIHHLHDSDFVHLSNLRVLNLKWNCPPAGLSPMHFPCRMTIEPNTFL	119
porcine	PRANVTSLSLLSNRIHHLHDSDFVHLSSLRTLNLKWNCPPAGLSPMHFPCHMTIEPNTFL	119
horse	PRDNVTSLSLLSNRIHHLHDSDFAQLSNLQKLNLKWNCPPAGLSPMHFPCHMTIEPNTFL	119
human	PRGNVTSLSLSSNRIHHLHDSDFAHLPSLRHLNLKWNCPPVGLSPMHFPCHMTIEPSTFL	120
rat .	PRSNITSLSLIANRIHHLHNLDFVHLPNVRQLNLKWNCPPPGLSPLHFSCRMTIEPKTFL	120
	** *:**** :******: **.:: :: ******** .**:*:*:****** ***	120

feline	AVPTIERIMI CYNCTOTUDA I DOGI MOLOLOGO COMPAZZATA DE MARIO	
canine	AVPTLEELNLSYNSITTVPALPSSLVSLSLSRTNILVLDPANLAGLHSLRFLFLDGNCYY AVPTLEDLNLSYNSITTVPALPSSLVSLSLSRTNILVLDPATLAGLYALRFLFLDGNCYY	180
bovine	AVPTLEELNI GYNCITTUDAL POGLAGI GOLGOLGOLGOLGOLGOLGOLGOLGOLGOLGOLGOLGOLG	180
mouse	AVPTLEELNLSYNGITTVPALPSSLVSLSLSHTSILVLGPTHFTGLHALRFLYMDGNCYY	179
ovine	AVPTLEELNLSYNGITTVPALPSSLVSLSLSHTSILVLGPTHFTGLHALRFLYMDGNCYY	179
porcine	AVPTLEELNLSYNGITTVPALPSSLVSLSLSRTSILVLGPTHFTGLHALRFLYMDGNCYY	179
horse	AVPTLEELNLSYNSITTVPALPDSLVSLSRTNILVLDPTHLTGLHALRYLYMDGNCYY	179
human	AVPTLEELNLSYNGITTVPALPSSLVSLILSRTNILQLDPTSLTGLHALRFLYMDGNCYY	180
rat	AVPTLEELNLSYNNIMTVPALPKSLISLSLSHTNILMLDSASLAGLHALRFLFMDGNCYY	180
Tac	AMRMLEELNLSYNGITTVPRLPSSLTNLSLSHTNILVLDASSLAGLHSLRVLFMDGNCYY	180
	*: **:*****.* *** **.** ** **.::::**::**	
feline	MIDCDONI OUNDONI I CI CUI MUI GI IGDUI TININI CI IGDUI TININI	
canine	KNPCPQALQVAPGALLGLGNLTHLSLKYNNLTAVPRGLPPSLEYLLLSYNHIITLAPEDL	240
bovine	KNPCQQALQVAPGALLGLGNLTHLSLKYNNLTVVPRGLPPSLEYLLLSYNHIITLAPEDL	240
mouse	MNPCPRALEVAPGALLGLGNLTHLSLKYNNLTEVPRRLPPSLDTLLLSYNHIVTLAPEDL	239
ovine	MNPCPRALEVAPGALLGLGNLTHLSLKYNNLTEVPRRLPPSLDTLLLSYNHIVTLAPEDL	239
porcine	KNPCQQAVEVAPGALLGLGNLTHLSLKYNNLTEVPRRLPPSLDTLLLSYNHIITLAPEDL	239
horse	KNPCQGALEVVPGALLGLGNLTHLSLKYNNLTEVPRSLPPSLETLLLSYNHIVTLTPEDL	239
human	KNPCGRALEVAPGALLGLGNLTHLSLKYNNLTTVPRSLPPSLEYLLLSYNHIVTLAPEDL	240
rat	KNPCRQALEVAPGALLGLGNLTHLSLKYNNLTVVPRNLPSSLEYLLLSYNRIVKLAPEDL	240
rat	KNPCNGAVNVTPDAFLGLSNLTHLSLKYNNLTEVPRQLPPSLEYLLLSYNLIVKLGAEDL	240
	*** *::*.*.********** *** **: ***** *:. * .**	
feline	AND THE DURONG THE PARTY OF THE	
canine	ANLTALRYLDVGGNCRRCDHARNPCMECPKGFPHLHPDTFSHLNHLEGLVLKDSSLYNLN	300
bovine	ANLTALRYLDVGGNCRRCDHARNPCRECPKGFPQLHPNTFGHLSHLEGLVLRDSSLYSLD	300
mouse	ANLTALRYLDVGGNCRRCDHARNPCRECPKNFPKLHPDTFSHLSRLEGLVLKDSSLYKLE	299
	ANLTALRYLDVGGNCRRCDHARNPCRECPKNFPKLHPDTFSHLSRLEGLVLKDSSLYKLE	299
ovine	ANLTALRYLDVGGNCRRCDHARNPCRECPKNFPKLHPDTFSHLSRLEGLVLKDSSLYKLE	299
porcine	ANLTALRYLDVGGNCRRCDHARNPCRECPKDHPKLHSDTFSHLSRLEGLVLKDSSLYNLD	299
horse	ANLTALRVLDVGGNCRRCDHARNPCVECPHKFPQLHSDTFSHLSRLEGLVLKDSSLYQLN	300
human	ANLTALRVLDVGGNCRRCDHAPNPCMECPRHFPQLHPDTFSHLSRLEGLVLKDSSLSWLN	300
rat	ANLTSLRMLDVGGNCRRCDHAPDLCTECRQKSLDLHPQTFHHLSHLEGLVLKDSSLHSLN	300
	****:************* : * ** : .**.:** **.:*****:*** *:	
folina	DOMESTA I CHI MII DI OMINI III CANTONI III	
feline	PRWFHALGNLMVLDLSENFLYDCITKTTAFQGLAQLRRLNLSFNYHKKVSFAHLHLAPSF	360
canine	PRWFHGLGNLMVLDLSENFLYDCITKTKAFYGLARLRRLNLSFNYHKKVSFAHLHLASSF	360
bovine	KDWFRGLGRLQVLDLSENFLYDYITKTTIFNDLTQLRRLNLSFNYHKKVSFAHLHLASSF	359
mouse	KDWFRGLGRLQVLDLSENFLYDYITKTTIFNDLTQLRRLNLSFNYHKKVSFAHLHLASSF	359
ovine	KDWFRGLGRLQVLDLSENFLYDYITKTTIFRNLTQLRRLNLSFNYHKKVSFAHLQLAPSF	359
porcine	TRWFRGLDRLQVLDLSENFLYDCITKTTAFQGLARLRSLNLSFNYHKKVSFAHLHLAPSF	359
horse	PRWFRGLGNLTVLDLSENFLYDCITKTKAFQGLAQLRRLNLSFNYHKKVSFAHLTLAPSF	360
human	ASWFRGLGNLRVLDLSENFLYKCITKTKAFQGLTQLRKLNLSFNYOKRVSFAHLSLAPSF	360
rat	SKWFQGLANLSVLDLSENFLYESINKTSAFONLTRLRKLDLSFNYCKKVSFARLHLASSF	360
	: * * ****** * ** * * * * * * * * *	

Figure 1 (2/3)

	• •
E-11	COLL OF OOL PARIOTERED OF CHAMILE OF THE PARIOTE OF COLUMN OF CHAMILE OF CHA
feline	GSLLSLQQLDMHGIFFRSLSETTLRSLVHLPMLQSLHLQMNFINQAQLSIFGAFPGLRYV 420
canine	GSLLSLQELDIHGIFFRSLSKTTLQSLAHLPMLQRLHLQLNFISQAQLSIFGAFPGLRYV 420
bovine	GSLVSLEKLDMHGIFFRSLTNITLQSLTRLPKLQSLHLQLNFINQAQLSIFGAFPSLLFV 419
mouse	GSLVSLEKLDMHGIFFRSLTNITLQSLTRLPKLQSLHLQLNFINQAQLSIFGAFPSLLFV 419
ovine	GGLVSLEKLDMHGIFFRSLTNTTLRPLTQLPKLQSLSLQLNFINQAELSIFGAFPSLLFV 419
porcine	GHLRSLKELDMHGIFFRSLSETTLQPLVQLPMLQTLRLQMNFINQAQLSIFGAFPGLLYV 419
horse	GSLLSLQELDMHGIFFRSLSQKTLQPLARLPMLQRLYLQMNFINQAQLGIFKDFPGLRYI 420
human	GSLVALKELDMHGIFFRSLDETTLRPLARLPMLQTLRLQMNFINQAQLGIFRAFPGLRYV 420
rat	KSLVSLQELNMNGIFFRLLNKNTLRWLAGLPKLHTLHLQMNFINQAQLSVFSTFRALRFV 420
	* :*::*::**** * : **: *. ** *: * **:***.**:* .:* * .* ::
feline	DLSDNRISGAMELAAATGEVDGGERVRLPSGDLALGPPGTPSSEGFMPGCKTLNFTLD 478
canine	DLSDNRISGAAEPAAATGEVEADCGERVWPQSRDLALGPLGTPGSEAFMPSCRTLNFTLD 480
bovine	DLSDNRISGAATPAAALGEVDSRVEVWRLPRGLAPGPLDAVSSKDFMPSCN-LNFTLD 476
mouse	DLSDNRISGAATPAAALGEVDSRVEVWRLPRGLAPGPLDAVSSKDFMPSCN-LNFTLD 476
ovine	DLSDNRISGAARPVAALGEVDSGVEVWRWPRGLAPGPLAAVSAKDFMPSCN-LNFTLD 476
porcine	DLSDNRISGAARPVAITREVDGRERVWLPSRNLAPRPLDTLRSEDFMPNCKAFSFTLD 477
horse	DLSDNRISGAVEPVATTGEVDGGKKVWLTSRDLTPGPLDTPSSEDFMPSCKNLSFTLD 478
human	DLSDNRISGASELTATMGEADGGEKVWLQPGDLAPAPVDTPSSEDFRPNCSTLNFTLD 478
rat	DLSNNRISGPPTLSRVAPEKAD-EAEKGVPWPASLTPALPSTPVSKNFMVRCKNLRFTMD 479
	:**.
feline	LSRNNLVTIQPEMFARLSRLQCLLLSRNSISQAVNGSQFMPLTSLQVLDLSHNKLDLYHG 538
canine	LSRNNLVTVQPEMFVRLARLQCLGLSHNSISQAVNGSQFVPLSNLRVLDLSHNKLDLYHG 540
bovine	LSRNNLVTIQQEMFTRLSRLQCLRLSHNSISQAVNGSQFVPLTSLRVLDLSHNKLDLYHG 536
mouse	LSRNNLVTIQQEMFTRLSRLQCLRLSHNSISQAVNGSQFVPLTSLRVLDLSHNKLDLYHG 536
ovine	LSRNNLVTIQQEMFTRLSRLQCLRLSHNSISQAVNGSQFVPLTRLRVLDLSYNKLDLYHG 536
porcine	LSRNNLVTIQSEMFARLSRLECLRLSHNSISQAVNGSQFVPLTSLRVLDLSHNKLDLYHG 537
horse	LSRNNLVTVQPEMFAQLSRLQCLRLSHNSISQAVNGSQFVPLTSLQVLDLSHNKLDLYHG 538
human	LSRNNLVTVQPEMFAQLSHLQCLRLSHNCISQAVNGSQFLPLTGLQVLDLSHNKLDLYHE 538
rat	LSRNNQVTIKPEMEVNLSHLQCLSLSHNCIAQAVNGSQFLPLTNLKVLDLSYNKLDLYHS 539
240	**** **: *** ** ** ** ** ** ** ** ** * * * * * *
feline	RSFTELPRLEALDLSYNSQPFSMQGVGHNLSFVAQLPALRYLSLAHNDIHSRVSQQLCSA 598
canine	RSFTELPRLEALDLSYNSOPFSMRGVGHNLSFVAQLPALRYLSLAHNGIHSRVSQQLRSA 600
bovine	RSFTELPOLEALDLSYNSOPFSMOGVGHNLSFVAQLPSLRYLSLAHNGIHSRVSQKLSSA 596
mouse	RSFTELPQLEALDLSYNSQPFSMQGVGHNLSFVAQLPSLRYLSLAHNGIHSRVSQKLSSA 596
ovine	RSFTELPOLEALDLSYNSOPFSMOGVGHNLSFVAOLPSLRYLSLAHNGIHSRVSQKLSSA 596
porcine	RSFTELPRLEALDLSYNSQPFTMQGVGHNLSFVAQLPALRYLSLAHNDIHSRVSQQLCSA 597
horse	RSFTELPRLEALDLSYNSQPFSMRGVGHNLSFVAQLPTLRYLSLAHNGIHSRVSQQLCST 598
human	HSFTELPRLEALDLSYNSQPFGMQGVGHNFSFVAHLRTLRHLSLAHNNIHSQVSQQLCST 598
rat	KSFSELPQLQALDLSYNSQPFSMQGIGHNFSFLANLSRLQNLSLAHNDIHSRVSSRLYST 599
Ide	**:***:********** *:*:**:**:* *: *******
feline	SLRALDFSGNALSRMWAEGDLYLHFFRGLRSLVRLDLSQNRLHTLLPRTLDNLPKSLRLL 658
canine	SLRALDFSGNTLSQMWAEGDLYLRFFQGLRSLVQLDLSQNRLHTLLPRNLDNLPKSLRLL 660
bovine	SLRALDFSGNSLSQMWAEGDLYLCFFKGLRNLVQLDLSENHLHTLLPRHLDNLPKSLRQL 656
	SLRALDFSGNSLSQMWAEGDLYLCFFKGLRNLVQLDLSENHLHTLLPRHLDNLPKSLRQL 656
mouse	SLRALDFSGNSLSQMWAEGDLYLCFFKGLRNLVQLDLSKNHLHTLLPRHLDNLPKSLRQL 656
ovine	SLCALDFSGNDLSRMWAEGDLYLRFFQGLRSLVWLDLSQNHLHTLLPRALDNLPKSLKHL 657
porcine	SLCADDFSGNSLSQMWAEGDLYLRFFQGLRSLIRLDLSQNRLHTLLPCTLGNLPKSLQLL 658
horse	SLRALDFSGNALGHMWAEGDLYLHFFQGLSGLIWLDLSQNRLHTLLPQTLRNLPKSLQVL 658
human	SVEYLDFSGNGVGRMWDEEDLYLYFFQDLRSLIHLDLSQNKLHILRPQNLNYLPKSLTKL 659
rat	*: ***** :::** * *** **: * : *** * * *
e-12	RLRDNYLAFFNWSSLVLLPRLEALDLAGNQLKALSNGSLPNGTQLQRLDLSSNSISFVAS 718
feline	RLRDNYLAFFNWSSLALLPKLEALDLAGNQLKALSNGSLFNGTQLQRLDLSGNSIGFVVP 720
canine	KEKUNILAKENWASHAHUKAHAHUHAGNUHKAHANGSHYMGIYUATUHAGNAHATAFA 720
bovine	RIRDNNIAFFNWSSLTVLPRLEALDLAGNQLKALSNGSLPPGIRLQKLDVSSNSIGFVIP 716
mouse	RLRONNLAFFNWSSLTVLPRLEALDLAGNQLKALSNGSLPPGIRLQKLDVSSNSIGFVIP 716
ovine	RLRDNNLAFFNWSSLTVLPQLEALDLAGNQLKALSNGSLPPGTRLQKLDVSSNSIGFVTP 716
porcine	HLRDNNLAFFNWSSLTLLPKLETLDLAGNQLKALSNGSLPSGTQLRRLDLSGNSIGFVNP 717
horse	RLRNNYLAFFNWSSLTLLPNLETLDLAGNQLKALSNGSLPSGTQLQRLDVSRNSIIFVVP 718
human	RLRDNYLAFFKWWSLHFLPKLEVLDLAGNQLKALTNGSLPAGTRLRRLDVSCNSISFVAP 718
rat	SFRONHLSFFNWSSLAFLPNLRDLDLAGNLLKALTNGTLPNGTLLQKLDVSSNSIVFVVP 719
	*** * *** * * * * * * * * * * * * * * *

WO 2004/026888 PCT/US2003/029577 3/4

Figure 1 (3/3)

feline	SFFALATRLRELNLSANALKTVEPSWFGSLAGTLKVLDVTGNPLHCACGAAFVDFLLEVQ	778
canine	SFFALAVRLRELNLSANALKTVEPSWFGSLAGALKVLDVTANPLHCACGATFVDFLLEVQ	780
bovine	GFFVRATRLIELNLSANALKTVDPSWFGSLAGTLKILDVSANPLHCACGAAFVDFLLERQ	776
mouse	CENTED A MINT THE LAST CONTROL OF	776
ovine	GFFVLANRLKELNLSANALKTVDPFWFGRLTETLNILDVSANPLHCACGAAFVDFLLEMO	776
porcine	GFFALAKQLEELNLSANALKTVEPSWFGSMVGNLKVLDVSANPLHCACGATFVGFLLEVQ	777
horse		
human	GFFSKAKELRELNLSANALKTVDHSWFGPLASALQILDVSANPLHCACGAAFMDFLLEVQ	778
rat	AFFALAVELKEVNLSHNILKTVDRSWFGPIVMNLTVLDVSSNPLHCACGAPFVDLLLEVQ	
	** * * * * * * * * * * * * * * * * * *	119
feline	AAVPGLPGHVKCGSPGQLQGRSIFAQDLRLCLDEALSWDCFGLSLLTVALGLAVPMLHHI	838
canine	AAVPGLPSRVKCGSPGQLQGRSIFAQDLRLCLDEALSWVCFSLSLLAVALSLAVPMLHQT	
		840
bovine	EAVPGLSRRVTCGSPGQLQGRSIFTQDLRLCLDETLSLDCFGLSLLMVALGLAVPMLHHI	836
mouse	EAVPGLSRRVTCGSPGQLQGRSIFTQDLRLCLDETLSLDCFGLSLLMVALGLAVPMLHHI	836
ovine	AAVPGLSRRVTCGSPGQLQGRSIFAQDLRLCLDETLSLDCFGFSLLMVALGLAVPMLHHI	836
porcine	AAVPGLPSRVKCGSPGQLQGHSIFAQDLRLCLDETLSWNCFGISLLAMALGLVVPMLHHL	837
horse	AAVPGLPSRVKCGSPGQLQGRSIFAQDLRLCLDKSLSWDCFGLSLLVVALGLAMPMLHHL	838
human	AAVPGLPSRVKCGSPGQLQGLSIFAQDLRLCLDEALSWDCFALSLLAVALGLGVPMLHHI	838
rat	TKVPGLANGVKCGSPRQLQGRSIFAQDLRLCLDDVLSRDCFGLSLLAVAVGTVLPLLQHI	839
	****	039
feline	CGWDLWYCFHLCLAWLPRRGRRRGADALPYDAFVVFDKAQSAVADWVYNELRVRLEER	000
canine	CGWDLWYCFHLCLAWLPRRGRRRGVDALAYDAFVVFDKAOSSVADWVYNELRVOLEER	
bovine		
mouse	CGWDLWYCFHLCLAHLPRRRRQRGEDTLLYDAVVVFDKVQSAVADWVYNELRVQLEER	
	CGWDLWYCFHLCLAHLPRRRRQRGEDTLLYDAVVVFDKVQSAVADWVYNELRVQLEER	
ovine	CGWDLWYCFHLCLAHLPRRRRQRGEDTLLYDAFVVFDKAQSAVADWVYNELRVQLEER	
porcine	CGWDLWYCFHLCLAWLPHRGQRRGADALFYDAFVVFDKAQSAVADWVYNELRVQLEER	
horse	CGWDLWYCFHLGLAWLPRRGWQRGADALSYDAFVVFDKAQSAVADWVYNELRVRLEER	
human	CGWDLWYCFHLCLAWLPWRGRQSGRDEDALPYDAFVVFDKTQSAVADWVYNELRGQLEEC	
rat	CGWDVWYCFHLCLAWLPLLTRGR-RSAQALPYDAFVVFDKAQSAVADWVYNELRVRLEER	898
	****:***** ** ** ** ::* ***.****.**:******* :***	
c		
feline	RGRRALRLCLEERDWLPGKTLFENLWASVYSSRKMLFVLAHTDRVSGLLRASFLLAQQRL	
canine	RGRRALRLCLEERDWVPGKTLFENLWASVYSSRKTLFVLARTDRVSGLLRASFLLAQQRL	
bovine	RGRRALRLCLEERDWLPGKTLFENLWASVYSSRKTMFVLDHTDRVSGLLRASFLLAQQRL	
mouse	RGRRALRLCLEERDWLPGKTLFENLWASVYSSRKTMFVLDHTDRVSGLLRASFLLAQQRL	
ovine	RGRRALRLCLEERDWLPGKTLFENLWASVYSSRKTMFVLDHTDRVSGLLRASFLLAQQRL	
porcine	RGRRALRLCLEERDWLPGKTLFENLWASVYSSRKTLFVLAHTDRVSGLLRASFLLAQQRL	
horse	RGRRALRLCLEERDWLPGKTLFENLWASVYSSRKMLFVLAHTDQVSGLLRASFLLAQQRL	
human	RGRWALRLCLEERDWLPGKTLFENLWASVYGSRKTLFVLAHTDRVSGLLRASFLLAQQRL	958
rat	RGRRALRLCLEDRDWLPGQTLFENLWASIYGSRKTLFVLAHTDKVSGLLRTSFLLAQQRL	958
	*** ******:***:********* :*** :*** :******	
feline	LEDRKDVVVLVILRPDAHRSRYVRLRQRLCRQSVLLWPHQPSGQRSFWAQLGTALTRDNQ	
canine	LEDRKDVVVLVILCPDAHRSRYVRLRQRLCRQSVLLWPHQPSGQRSFWAQLGTALTRDNR	
bovine	LEDRKDVVVLVILRPAAYRSRYVRLRQRLCRQSVLLWPHQPSGQGSFWANLGIALTRDNR	
mouse	LEDRKDVVVLVILRPAAYRSRYVRLRQRLCRQSVLLWPHQPSGQGSFWANLGIALTRDNR	
ovine	LEDRKDVVVLVILRPAAYRSRYVRLRQRLCRQSVLLWPHQPSGQGSFWANLGMALTRDNR	
porcine	LEDRKDVVVLVILRPDAYRSRYVRLRQRLCRQSVLLWPHQPRGQGSFWAQLGTALTRDNH	1015
horse	LEDRKDVVVLVILSPDARRSRYVRLRQRLCRQSVLFWPHQPSGQRSFWAQLGMALTRDNR	1016
human	LEDRKDVVVLVILSPDGRRSRYVRLRQRLCRQSVLLWPHQPSGQRSFWAQLGMALTRDNH	1018
rat	LEDRKDVVVLVILRPDAHRSRYVRLRQRLCRQSVLFWPHQPNGQGSFWAQLSTALTRDNH	1018
	********* * . ************* ** ** ***: * . *****:	
feline	HFYNQNFCRGPTTAE	
canine	HFYNQNFCRGPTTA	1032
bovine	HFYNRNFCRGPTTAE	
mouse	HFYNRNFCRGPTTAE	1032
ovine	HFYNRNFCRGPTTAE	1029
porcine	HFYNRNFCRGPTTAE	
horse	HFYNQNFCRGPTMAE	1031
human	HFYNRNFCQGPTAE	
rat	HFYNRNFCRGPTAE	1032
	****:***	

Figure 2

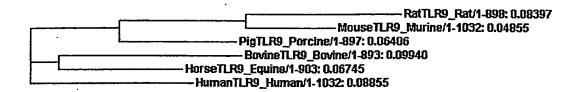
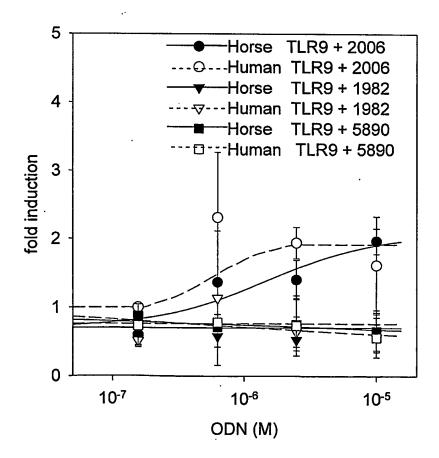


Figure 3



SEQUENCE LISTING

<110> Coley Pharmaceutical GmbH University of Saskatchewan Qiagen GmbH

- <120> TOLL-LIKE RECEPTOR 9 (TLR9) FROM VARIOUS MAMMALIAN SPECIES
- <130> C1041.70040WO00
- <150> US 60/412,479
- <151> 2002-09-19
- <160> 70
- <170> PatentIn version 3.1
- <210> 1

- <211> 1032 <212> PRT <213> Rattus norvegicus
- <400> 1

Met Val Leu Cys Arg Arg Thr Leu His Pro Leu Ser Leu Leu Val Gln 5

Ala Ala Val Leu Ala Glu Ala Leu Ala Leu Gly Thr Leu Pro Ala Phe 25

Leu Pro Cys Glu Leu Lys Pro His Gly Leu Val Asp Cys Asn Trp Leu 35 45

Phe Leu Lys Ser Val Pro His Phe Ser Ala Ala Glu Pro Arg Ser Asn 50

Ile Thr Ser Leu Ser Leu Ile Ala Asn Arg Ile His His Leu His Asn 70

Leu Asp Phe Val His Leu Pro Asn Val Arg Gln Leu Asn Leu Lys Trp

Asn Cys Pro Pro Pro Gly Leu Ser Pro Leu His Phe Ser Cys Arg Met 100 110

Thr Ile Glu Pro Lys Thr Phe Leu Ala Met Arg Met Leu Glu Glu Leu 115 120

Asn Leu Ser Tyr Asn Gly Ile Thr Thr Val Pro Arg Leu Pro Ser Ser 130 135 140

Leu Thr Asn Leu Ser Leu Ser His Thr Asn Ile Leu Val Leu Asp Ala 150 155 Ser Ser Leu Ala Gly Leu His Ser Leu Arg Val Leu Phe Met Asp Gly Asn Cys Tyr Tyr Lys Asn Pro Cys Asn Gly Ala Val Asn Val Thr Pro 185 Asp Ala Phe Leu Gly Leu Ser Asn Leu Thr His Leu Ser Leu Lys Tyr 200 Asn Asn Leu Thr Glu Val Pro Arg Gln Leu Pro Pro Ser Leu Glu Tyr Leu Leu Leu Ser Tyr Asn Leu Ile Val Lys Leu Gly Ala Glu Asp Leu 230 Ala Asn Leu Thr Ser Leu Arg Met Leu Asp Val Gly Gly Asn Cys Arg , 245 250 Arg Cys Asp His Ala Pro Asp Leu Cys Thr Glu Cys Arg Gln Lys Ser Leu Asp Leu His Pro Gln Thr Phe His His Leu Ser His Leu Glu Gly 280 Leu Val Leu Lys Asp Ser Ser Leu His Ser Leu Asn Ser Lys Trp Phe 295 Gln Gly Leu Ala Asn Leu Ser Val Leu Asp Leu Ser Glu Asn Phe Leu Tyr Glu Ser Ile Asn Lys Thr Ser Ala Phe Gln Asn Leu Thr Arg Leu 330 Arg Lys Leu Asp Leu Ser Phe Asn Tyr Cys Lys Lys Val Ser Phe Ala 345 Arg Leu His Leu Ala Ser Ser Phe Lys Ser Leu Val Ser Leu Gln Glu 360 Leu Asn Met Asn Gly Ile Phe Phe Arg Leu Leu Asn Lys Asn Thr Leu 375 380

Arg Trp Leu Ala Gly Leu Pro Lys Leu His Thr Leu His Leu Gln Met 385 390 395 400

- Asn Phe Ile Asn Gln Ala Gln Leu Ser Val Phe Ser Thr Phe Arg Ala 405 410 415
- Leu Arg Phe Val Asp Leu Ser Asn Asn Arg Ile Ser Gly Pro Pro Thr 420 425 430
- Leu Ser Arg Val Ala Pro Glu Lys Ala Asp Glu Ala Glu Lys Gly Val 435 440 445
- Pro Trp Pro Ala Ser Leu Thr Pro Ala Leu Pro Ser Thr Pro Val Ser 450 455 460
- Lys Asn Phe Met Val Arg Cys Lys Asn Leu Arg Phe Thr Met Asp Leu 465 470 475 480
- Ser Arg Asn Asn Gln Val Thr Ile Lys Pro Glu Met Phe Val Asn Leu 485 490 495
- Ser His Leu Gln Cys Leu Ser Leu Ser His Asn Cys Ile Ala Gln Ala
 500 505 510
- Val Asn Gly Ser Gln Phe Leu Pro Leu Thr Asn Leu Lys Val Leu Asp 515 520 525
- Leu Ser Tyr Asn Lys Leu Asp Leu Tyr His Ser Lys Ser Phe Ser Glu 530 535 540
- Leu Pro Gln Leu Gln Ala Leu Asp Leu Ser Tyr Asn Ser Gln Pro Phe 545 550 555 560
- Ser Met Gln Gly Ile Gly His Asn Phe Ser Phe Leu Ala Asn Leu Ser 565 570 575
- Arg Leu Gln Asn Leu Ser Leu Ala His Asn Asp Ile His Ser Arg Val 580 585 590
- Ser Ser Arg Leu Tyr Ser Thr Ser Val Glu Tyr Leu Asp Phe Ser Gly 595 600 605
- Asn Gly Val Gly Arg Met Trp Asp Glu Glu Asp Leu Tyr Leu Tyr Phe

610 615 620

Phe Gln Asp Leu Arg Ser Leu Ile His Leu Asp Leu Ser Gln Asn Lys 625 630 635

Leu His Ile Leu Arg Pro Gln Asn Leu Asn Tyr Leu Pro Lys Ser Leu 645 650 655

Thr Lys Leu Ser Phe Arg Asp Asn His Leu Ser Phe Phe Asn Trp Ser 660 665 670

Ser Leu Ala Phe Leu Pro Asn Leu Arg Asp Leu Asp Leu Ala Gly Asn 675 680 685

Leu Leu Lys Ala Leu Thr Asn Gly Thr Leu Pro Asn Gly Thr Leu Leu 690 695 700

Gln Lys Leu Asp Val Ser Ser Asn Ser Ile Val Phe Val Val Pro Ala 705 710 715 720

Phe Phe Ala Leu Ala Val Glu Leu Lys Glu Val Asn Leu Ser His Asn 725 730 735

Ile Leu Lys Thr Val Asp Arg Ser Trp Phe Gly Pro Ile Val Met Asn 740 745 750

Leu Thr Val Leu Asp Val Ser Ser Asn Pro Leu His Cys Ala Cys Gly 755 760 765

Ala Pro Phe Val Asp Leu Leu Glu Val Gln Thr Lys Val Pro Gly 770 780

Leu Ala Asn Gly Val Lys Cys Gly Ser Pro Arg Gln Leu Gln Gly Arg
785 790 795 800

Ser Ile Phe Ala Gln Asp Leu Arg Leu Cys Leu Asp Asp Val Leu Ser 805 810 815

Arg Asp Cys Phe Gly Leu Ser Leu Leu Ala Val Ala Val Gly Thr Val 820 825 830

Leu Pro Leu Gln His Leu Cys Gly Trp Asp Val Trp Tyr Cys Phe 835 840 845

His Leu Cys Leu Ala Trp Leu Pro Leu Eu Thr Arg Gly Arg Arg Ser 850 855

Ala Gln Ala Leu Pro Tyr Asp Ala Phe Val Val Phe Asp Lys Ala Gln 865 870 875 880

Ser Ala Val Ala Asp Trp Val Tyr Asn Glu Leu Arg Val Arg Leu Glu 885 890 895

Glu Arg Arg Gly Arg Arg Ala Leu Arg Leu Cys Leu Glu Asp Arg Asp 900 905 910

Trp Leu Pro Gly Gln Thr Leu Phe Glu Asn Leu Trp Ala Ser Ile Tyr 915 920 925

Gly Ser Arg Lys Thr Leu Phe Val Leu Ala His Thr Asp Lys Val Ser 930 935 940

Gly Leu Leu Arg Thr Ser Phe Leu Leu Ala Gln Gln Arg Leu Leu Glu 945 950 955 960

Asp Arg Lys Asp Val Val Val Leu Val Ile Leu Arg Pro Asp Ala His 965 970 975

Arg Ser Arg Tyr Val Arg Leu Arg Gln Arg Leu Cys Arg Gln Ser Val 980 985 990

Leu Phe Trp Pro His Gln Pro Asn Gly Gln Gly Ser Phe Trp Ala Gln 995 1000 1005

Leu Ser Thr Ala Leu Thr Arg Asp Asn His His Phe Tyr Asn Arg 1010 1015 1020

Asn Phe Cys Arg Gly Pro Thr Ala Glu 1025 1030

<210> 2

<211> 821

<212> PRT

<213> Rattus norvegicus

<400> 2

Met Val Leu Cys Arg Arg Thr Leu His Pro Leu Ser Leu Leu Val Gln
1 5 10 15

Ala Ala Val Leu Ala Glu Ala Leu Ala Leu Gly Thr Leu Pro Ala Phe 20 25 30

Leu Pro Cys Glu Leu Lys Pro His Gly Leu Val Asp Cys Asn Trp Leu 35 40 45

Phe Leu Lys Ser Val Pro His Phe Ser Ala Ala Glu Pro Arg Ser Asn 50 55 60

Ile Thr Ser Leu Ser Leu Ile Ala Asn Arg Ile His His Leu His Asn 65 70 75 80

Leu Asp Phe Val His Leu Pro Asn Val Arg Gln Leu Asn Leu Lys Trp 85 90 95

Asn Cys Pro Pro Pro Gly Leu Ser Pro Leu His Phe Ser Cys Arg Met 100 105 110

Thr Ile Glu Pro Lys Thr Phe Leu Ala Met Arg Met Leu Glu Glu Leu 115 120 125

Asn Leu Ser Tyr Asn Gly Ile Thr Thr Val Pro Arg Leu Pro Ser Ser 130 140

Leu Thr Asn Leu Ser Leu Ser His Thr Asn Ile Leu Val Leu Asp Ala 145 150 155 160

Ser Ser Leu Ala Gly Leu His Ser Leu Arg Val Leu Phe Met Asp Gly 165 170 175

. . .

Asn Cys Tyr Tyr Lys Asn Pro Cys Asn Gly Ala Val Asn Val Thr Pro 180 185 190

Asp Ala Phe Leu Gly Leu Ser Asn Leu Thr His Leu Ser Leu Lys Tyr 195 200 205

Asn Asn Leu Thr Glu Val Pro Arg Gln Leu Pro Pro Ser Leu Glu Tyr 210 215 220

Leu Leu Ser Tyr Asn Leu Ile Val Lys Leu Gly Ala Glu Asp Leu 225 235 240

Ala Asn Leu Thr Ser Leu Arg Met Leu Asp Val Gly Gly Asn Cys Arg
245 250 255

Arg Cys Asp His Ala Pro Asp Leu Cys Thr Glu Cys Arg Gln Lys Ser 260 265 270

- Leu Asp Leu His Pro Gln Thr Phe His His Leu Ser His Leu Glu Gly 275 280 285
- Leu Val Leu Lys Asp Ser Ser Leu His Ser Leu Asn Ser Lys Trp Phe 290 295 300
- Gln Gly Leu Ala Asn Leu Ser Val Leu Asp Leu Ser Glu Asn Phe Leu 305 310 315 320
- Tyr Glu Ser Ile Asn Lys Thr Ser Ala Phe Gln Asn Leu Thr Arg Leu 325 330 335
- Arg Lys Leu Asp Leu Ser Phe Asn Tyr Cys Lys Lys Val Ser Phe Ala 340 345 350
- Arg Leu His Leu Ala Ser Ser Phe Lys Ser Leu Val Ser Leu Gln Glu 355 360 365
- Leu Asn Met Asn Gly Ile Phe Phe Arg Leu Leu Asn Lys Asn Thr Leu 370 380
- Arg Trp Leu Ala Gly Leu Pro Lys Leu His Thr Leu His Leu Gln Met 385 390 400
- Asn Phe Ile Asn Gln Ala Gln Leu Ser Val Phe Ser Thr Phe Arg Ala 405 410 415
- Leu Arg Phe Val Asp Leu Ser Asn Asn Arg Ile Ser Gly Pro Pro Thr 420 425 430
- Leu Ser Arg Val Ala Pro Glu Lys Ala Asp Glu Ala Glu Lys Gly Val 435 440 445
- Pro Trp Pro Ala Ser Leu Thr Pro Ala Leu Pro Ser Thr Pro Val Ser 450
- Lys Asn Phe Met Val Arg Cys Lys Asn Leu Arg Phe Thr Met Asp Leu 470 470 470 480
- Ser Arg Asn Asn Gln Val Thr Ile Lys Pro Glu Met Phe Val Asn Leu 485 490 495

Ser His Leu Gln Cys Leu Ser Leu Ser His Asn Cys Ile Ala Gln Ala 500 505 510

- Val Asn Gly Ser Gln Phe Leu Pro Leu Thr Asn Leu Lys Val Leu Asp 515 520 525
- Leu Ser Tyr Asn Lys Leu Asp Leu Tyr His Ser Lys Ser Phe Ser Glu 530 535 540
- Leu Pro Gln Leu Gln Ala Leu Asp Leu Ser Tyr Asn Ser Gln Pro Phe 545 550 555 560
- Ser Met Gln Gly Ile Gly His Asn Phe Ser Phe Leu Ala Asn Leu Ser 565 570 575
- Arg Leu Gln Asn Leu Ser Leu Ala His Asn Asp Ile His Ser Arg Val 580 585 590
- Ser Ser Arg Leu Tyr Ser Thr Ser Val Glu Tyr Leu Asp Phe Ser Gly 595 600 605
- Asn Gly Val Gly Arg Met Trp Asp Glu Glu Asp Leu Tyr Leu Tyr Phe 610 615 620
- Phe Gln Asp Leu Arg Ser Leu Ile His Leu Asp Leu Ser Gln Asn Lys 625 630 635 640
- Leu His Ile Leu Arg Pro Gln Asn Leu Asn Tyr Leu Pro Lys Ser Leu 645 650 655
- Thr Lys Leu Ser Phe Arg Asp Asn His Leu Ser Phe Phe Asn Trp Ser 660 665 670
- Ser Leu Ala Phe Leu Pro Asn Leu Arg Asp Leu Asp Leu Ala Gly Asn 675 680 685
- Leu Leu Lys Ala Leu Thr Asn Gly Thr Leu Pro Asn Gly Thr Leu Leu 690 695 700
- Gln Lys Leu Asp Val Ser Ser Asn Ser Ile Val Phe Val Val Pro Ala
 705 710 715 720
- Phe Phe Ala Leu Ala Val Glu Leu Lys Glu Val Asn Leu Ser His Asn

725 730 735

Leu Thr Val Leu Asp Val Ser Ser Asn Pro Leu His Cys Ala Cys Gly
755 760 765

Ala Pro Phe Val Asp Leu Leu Glu Val Gln Thr Lys Val Pro Gly 770 780

Leu Ala Asn Gly Val Lys Cys Gly Ser Pro Arg Gln Leu Gln Gly Arg
785 790 795 800

Ser Ile Phe Ala Gln Asp Leu Arg Leu Cys Leu Asp Asp Val Leu Ser 805 810 815

Arg Asp Cys Phe Gly 820

<210> 3

<211> 3099

<212> DNA

<213> Rattus norvegicus

<400> 3

atggttetet gtegeaggae cetgeacece ttgtetetec tggtacagge egeagtgetg 60 gctgaggctc tggccctggg taccctgcct gccttcctac cctgtgaact gaagcctcat 120 ggcctggtag actgcaactg gctcttcctg aagtctgtgc ctcacttctc tgccgcagaa 180 ccccgttcca acatcaccag cctttccttg atcgccaacc gcatccacca cctgcacaac 240 ctcgactttg tccacctgcc caacgtgcga cagctgaacc tcaagtggaa ctgtccgccc 300 cetggeetea geceettgea etteteetge egeatgacea ttgageecaa aacetteetg 360 gctatgcgca tgctggaaga gctgaacctg agctataacg gtatcaccac tgtgccccgc 420 ctgcccagct ccctgacgaa tctgagccta agccacacca acatcctggt actcgatgcc 480 agcagecteg etggeetgea eageetgega gttetettea tggaegggaa etgetaetae 540 aagaacccct gcaacggggc ggtgaacgtg accccggacg ccttcctggg cttgagcaac 600 ctcacccact tgtcccttaa gtataacaac ctcacagagg tgccccgcca actgcccccc 660 agectggagt acctectget gtectataac etcategtea agetggggge egaagaceta 720 gccaacctga cctcccttcg aatgcttgat gtgggtggga attgccgtcg ctgtgatcac 780

gccccgacc	tctgtacaga	atgccggcag	aagtcccttg	atctgcaccc	tcagactttc	840
catcacctga	gccaccttga	aggcctggtg	ctgaaggaca	gttctctcca	ctcgctgaac	900
tccaagtggt	tccagggtct	ggcgaacctc	tcggtgctgg	acctaagcga	gaactttctc	960
tacgagagca	tcaacaaaac	cagcgccttt	cagaacctga	cccgtctgcg	caagctcgac	1020
ctgtccttca	attactgcaa	gaaggtatcg	ttcgcccgcc	tccacctggc	aagttccttc	1080
aagagcctgg	tgtcgctgca	ggagctgaac	atgaacggca	tcttcttccg	cttactcaac	1140
aagaacacgc	tcaggtggct	ggctggtctg	cccaagctcc	acacgctgca	ccttcaaatg	1200
aatttcatca	accaggcgca	gctcagcgtc	tttagtacct	tecgagecet	tcgctttgtg	1260
gacctgtcca	ataatcgcat	cagcgggcct	ccaacgctgt	ccagagtcgc	ccccgaaaag	1320
gcagacgagg	cggagaaggg	ggttccatgg	cctgcaagtc	tcaccccagc	tctcccgagc	1380
actcccgtct	caaagaactt	catggtcagg	tgtaagaacc	tcagattcac	catggacctg	1440
tctcggaaca	accaggtgac	tatcaagcca	gagatgttcg	tcaacctctc	ccatctccag	1500
tgtctgagcc	tgagccacaa	ctgcatcgcg	caggctgtca	atggctctca	gttcctgccg	1560
ctgaccaacc	tgaaggtgct	ggacctgtcc	tataacaagc	tggacctgta	ccattcgaaa	1620
tcgttcagtg	agctcccaca	gttgcaggcc	ctggacctga	gctacaacag	ccagccattc	1680
agcatgcagg	ggataggcca	caacttcagt	tttctggcca	atctgtccag	gttacagaac	1740
cttagcctgg	cacacaatga	cattcacagc	cgcgtgtcct	cacgcctcta	cagcacctca	1800
gtggagtatc	tggacttcag	cggcaacggt	gtgggccgca	tgtgggacga	ggaggacctt	1860
tacctctatt	tcttccaaga	cctgagaagc	ctgattcatc	tggacctgtc	tcagaataag	1920
ctgcacatcc	tccggcccca	gaacctcaac	tacctcccca	agagcctgac	gaagctgagt	1980
ttccgtgaca	atcacctctc	tttctttaac	tggagcagtc	tggccttcct	gcccaatctg	2040
cgagacctgg	acctggcagg	caatctacta	aaggccctga	ccaacggcac	cctgcctaat	2100
ggcacgctcc	tccagaaact	ggatgtcagt	agcaacagta	tcgtctttgt	ggtcccagcc	2160
ttatttgata	tggcggtaga	gctaaaagag	gtcaacctca	gccataacat	cctcaagact	2220
gtggatcgct	cctggtttgg	gcccattgtg	atgaacctga	cggttctaga	cgtgagcagc	2280
aaccetetge	attgtgcctg	cggtgcaccc	tttgtagact	tactgctgga	agtgcagacc	2340
aaggtgcctg	gcctggctaa	cggtgtgaag	tgtggcagtc	cccgccagct	gcagggccgc	2400
agcatctttg	cgcaagacct	gcggctgtgc	ctggatgacg	tectttctcg	ggactgcttt	2460
ggcctttcac	tcctggctgt	ggccgtgggc	acggtgttgc	ctttactgca	gcatctctgc	2520
ggctgggacg	tctggtactg	tttccatctg	tgcctggcat	ggctaccttt	gctgacccgt	2580

724

2640 ggccggcgca gcgcccaagc tetecettat gatgcettcg tggtgttcga taaggcgcag agcgcggttg ctgactgggt gtataacgag cttcgagtgc ggctagagga gcggcgcggt 2700 cgccgagece taegettgtg tetggaggae egagattgge tgcctggeea gaeaetette 2760 2820 gagaacctct gggcctccat ctatggcagc cgcaagactc tgtttgtgct ggcccacacg 2880 gacaaggtca gtggcctcct gcgcaccagc ttcctgctgg ctcagcagcg cctgctggag gaccgcaagg acgtggtggt gttggtgatc ctgcgccctg atgcccaccg ctcccgctac 2940 gtgcgactgc gccagcgcct ctgccgccag agtgtgctct tctggcccca tcagcccaac 3000 gggcagggca gcttctgggc ccagctgagt acagccctga ctagggacaa ccaccacttc 3060 3099 tataaccgga acttctgccg gggacctaca gcagaatag

<210> 4

<211> 2463

<212> DNA

<213> Rattus norvegicus

<400> 4 60 atgqttctct qtcqcaggac cctgcacccc ttgtctctcc tggtacaggc cgcagtgctg getgaggete tggceetggg taccetgeet geetteetae eetgtgaact gaageeteat 120 ggcctggtag actgcaactg gctcttcctg aagtctgtgc ctcacttctc tgccgcagaa 180 ccccgttcca acatcaccag cctttccttg atcgccaacc gcatccacca cctgcacaac 240 ctcgactttg tccacctgcc caacgtgcga cagctgaacc tcaagtggaa ctgtccgccc 300 360 cctggcctca gccccttgca cttctcctgc cgcatgacca ttgagcccaa aaccttcctg gctatgcgca tgctggaaga gctgaacctg agctataacg gtatcaccac tgtgccccgc 420 ctgcccagct ccctgacgaa tctgagccta agccacacca acatcctggt actcgatgcc 480 agcagcctcg ctggcctgca cagcctgcga gttctcttca tggacgggaa ctgctactac 540 600 aagaacccct gcaacggggc ggtgaacgtg accccggacg ccttcctggg cttgagcaac ctcacccact tgtcccttaa gtataacaac ctcacagagg tgccccgcca actgcccccc 660 agcctggagt acctcctgct gtcctataac ctcatcgtca agctgggggc cgaagaccta 720 780 gccaacctga cctcccttcg aatgcttgat gtgggtggga attgccgtcg ctgtgatcac geocegace tetgtacaga atgeoggeag aagteeettg atetgcacee teagaettte 840 900 catcacctga gccaccttga aggcctggtg ctgaaggaca gttctctcca ctcgctgaac 960 tecaagtggt tecagggtet ggegaacete teggtgetgg acetaagega gaactteete tacgagagca tcaacaaaac cagcgccttt cagaacctga cccgtctgcg caagctcgac 1020

ctgtccttca	attactgcaa	gaaggtatcg	ttcgcccgcc	tccacctggc	aagttccttc	1080
aagagcctgg	tgtcgctgca	ggagctgaac	atgaacggca	tettetteeg	cttactcaac	1140
aagaacacgc	tcaggtggct	ggctggtctg	cccaagetcc	acacgctgca	ccttcaaatg	1200
aatttcatca	accaggcgca	gctcagcgtc	tttagtacct	teegageeet	tcgctttgtg	1260
gacctgtcca	ataatcgcat	cagcgggcct	ccaacgctgt	ccagagtcgc	ccccgaaaag	1320
gcagacgagg	cggagaaggg	ggttccatgg	cctgcaagtc	tcaccccagc	tctcccgagc	1380
actcccgtct	caaagaactt	catggtcagg	tgtaagaacc	tcagattcac	catggacctg	1440
tctcggaaca	accaggtgac	tatcaagcca	gagatgttcg	tcaacctctc	ccatctccag	1500
tgtctgagcc	tgagccacaa	ctgcatcgcg	caggctgtca	atggctctca	gttcctgccg	1560
ctgaccaacc	tgaaggtgct	ggacctgtcc	tataacaagc	tggacctgta	ccattcgaaa	1620
tcgttcagtg	agctcccaca	gttgcaggcc	ctggacctga	gctacaacag	ccagccattc	1680
agcatgcagg	ggataggcca	caacttcagt	tttctggcca	atctgtccag	gttacagaac	1740
cttagcctgg	cacacaatga	cattcacage	cgcgtgtcct	cacgcctcta	cagcacctca	1800
gtggagtatc	tggacttcag	cggcaacggt	gtgggccgca	tgtgggacga	ggaggacctt	1860
tacctctatt	tcttccaaga	cctgagaagc	ctgattcatc	tggacctgtc	tcagaataag	1920
ctgcacatcc	tccggcccca	gaacctcaac	tacctcccca	agagcctgac	gaagctgagt	1980
ttccgtgaca	atcacctctc	tttctttaac	tggagcagtc	tggccttcct	gcccaatctg	2040
cgagacctgg	acctggcagg	caatctacta	aaggccctga	ccaacggcac	cctgcctaat	2100
ggcacgctcc	tccagaaact	ggatgtcagt	agcaacagta	tcgtctttgt	ggtcccagcc	2160
ttetttgete	tggcggtaga	gctaaaagag	gtcaacctca	gccataacat	cctcaagact	2220
gtggatcgct	cctggtttgg	gcccattgtg	atgaacctga	cggttctaga	cgtgagcagc	2280
aaccctctgc	attgtgcctg	cggtgcaccc	tttgtagact	tactgctgga	agtgcagacc	2340
aaggtgcctg	gcctggctaa	cggtgtgaag	tgtggcagtc	cccgccagct	gcagggccgc	2400
agcatctttg	cgcaagacct	gcggctgtgc	ctggatgacg	tcctttctcg	ggactgcttt	2460
ggc						2463
			ŧ			

. . . .

<210> 5 <211> 1030 <212> PRT <213> Sus scrofa

<400> 5

Met Gly Pro Arg Cys Thr Leu His Pro Leu Ser Leu Leu Val Gln Val 1 5 10 15

- Thr Ala Leu Ala Ala Leu Ala Gln Gly Arg Leu Pro Ala Phe Leu 20 25 30
- Pro Cys Glu Leu Gln Pro His Gly Leu Val Asn Cys Asn Trp Leu Phe 35 40 45
- Leu Lys Ser Val Pro His Phe Ser Ala Ala Ala Pro Arg Ala Asn Val 50 60
- Thr Ser Leu Ser Leu Leu Ser Asn Arg Ile His His Leu His Asp Ser 65 70 75 80
- Asp Phe Val His Leu Ser Ser Leu Arg Thr Leu Asn Leu Lys Trp Asn 85 90 95
- Cys Pro Pro Ala Gly Leu Ser Pro Met His Phe Pro Cys His Met Thr 100 105 110
- Ile Glu Pro Asn Thr Phe Leu Ala Val Pro Thr Leu Glu Glu Leu Asn 115 120 125
- Leu Ser Tyr Asn Ser Ile Thr Thr Val Pro Ala Leu Pro Asp Ser Leu 130 135 140
- Val Ser Leu Ser Leu Ser Arg Thr Asn Ile Leu Val Leu Asp Pro Thr 145 150 155 160
- His Leu Thr Gly Leu His Ala Leu Arg Tyr Leu Tyr Met Asp Gly Asn 165 170 175
- Cys Tyr Tyr Lys Asn Pro Cys Gln Gly Ala Leu Glu Val Val Pro Gly 180 185 190
- Ala Leu Leu Gly Leu Gly Asn Leu Thr His Leu Ser Leu Lys Tyr Asn 195 200 205
- Asn Leu Thr Glu Val Pro Arg Ser Leu Pro Pro Ser Leu Glu Thr Leu 210 215 220
- Leu Leu Ser Tyr Asn His Ile Val Thr Leu Thr Pro Glu Asp Leu Ala 225 230 235 240

Asn Leu Thr Ala Leu Arg Val Leu Asp Val Gly Gly Asn Cys Arg Arg 255

- Cys Asp His Ala Arg Asn Pro Cys Arg Glu Cys Pro Lys Asp His Pro 260 265 270
- Lys Leu His Ser Asp Thr Phe Ser His Leu Ser Arg Leu Glu Gly Leu 275 280 285
- Val Leu Lys Asp Ser Ser Leu Tyr Asn Leu Asp Thr Arg Trp Phe Arg 290 295 300
- Gly Leu Asp Arg Leu Gln Val Leu Asp Leu Ser Glu Asn Phe Leu Tyr 305 310 315 320
- Asp Cys Ile Thr Lys Thr Thr Ala Phe Gln Gly Leu Ala Arg Leu Arg 325 330 335
- Ser Leu Asn Leu Ser Phe Asn Tyr His Lys Lys Val Ser Phe Ala His 340 345 350
- Leu His Leu Ala Pro Ser Phe Gly His Leu Arg Ser Leu Lys Glu Leu 355 360 365
- Asp Met His Gly Ile Phe Phe Arg Ser Leu Ser Glu Thr Thr Leu Gln 370 380
- Pro Leu Val Gln Leu Pro Met Leu Gln Thr Leu Arg Leu Gln Met Asn 385 390 395 400
- Phe Ile Asn Gln Ala Gln Leu Ser Ile Phe Gly Ala Phe Pro Gly Leu 405 410 415
- Leu Tyr Val Asp Leu Ser Asp Asn Arg Ile Ser Gly Ala Ala Arg Pro 420 425 430
- Val Ala Ile Thr Arg Glu Val Asp Gly Arg Glu Arg Val Trp Leu Pro 435 440 445
- Ser Arg Asn Leu Ala Pro Arg Pro Leu Asp Thr Leu Arg Ser Glu Asp 450 455 460
- Phe Met Pro Asn Cys Lys Ala Phe Ser Phe Thr Leu Asp Leu Ser Arg
 470 475 480

Asn Asn Leu Val Thr Ile Gln Ser Glu Met Phe Ala Arg Leu Ser Arg 485 490 495

- Leu Glu Cys Leu Arg Leu Ser His Asn Ser Ile Ser Gln Ala Val Asn 500 505 510
- Gly Ser Gln Phe Val Pro Leu Thr Ser Leu Arg Val Leu Asp Leu Ser 515 520 525
- His Asn Lys Leu Asp Leu Tyr His Gly Arg Ser Phe Thr Glu Leu Pro 530 540
- Arg Leu Glu Ala Leu Asp Leu Ser Tyr Asn Ser Gln Pro Phe Thr Met 545 550 555 560
- Gln Gly Val Gly His Asn Leu Ser Phe Val Ala Gln Leu Pro Ala Leu 565 570 575
- Arg Tyr Leu Ser Leu Ala His Asn Asp Ile His Ser Arg Val Ser Gln 580 585 585
- Gln Leu Cys Ser Ala Ser Leu Cys Ala Leu Asp Phe Ser Gly Asn Asp 595 600 605
- Leu Ser Arg Met Trp Ala Glu Gly Asp Leu Tyr Leu Arg Phe Phe Gln 610 615 620
- Gly Leu Arg Ser Leu Val Trp Leu Asp Leu Ser Gln Asn His Leu His 625 630 640
- Thr Leu Leu Pro Arg Ala Leu Asp Asn Leu Pro Lys Ser Leu Lys His 645 650 655
- Leu His Leu Arg Asp Asn Asn Leu Ala Phe Phe Asn Trp Ser Ser Leu 660 665 670
- Thr Leu Leu Pro Lys Leu Glu Thr Leu Asp Leu Ala Gly Asn Gln Leu 675 680 685
- Lys Ala Leu Ser Asn Gly Ser Leu Pro Ser Gly Thr Gln Leu Arg Arg 690 695 700
- Leu Asp Leu Ser Gly Asn Ser Ile Gly Phe Val Asn Pro Gly Phe Phe

705 710 715 720

Ala Leu Ala Lys Gln Leu Glu Glu Leu Asn Leu Ser Ala Asn Ala Leu 725 730 735

Lys Thr Val Glu Pro Ser Trp Phe Gly Ser Met Val Gly Asn Leu Lys 740 745 750

Val Leu Asp Val Ser Ala Asn Pro Leu His Cys Ala Cys Gly Ala Thr 755 760 765

Phe Val Gly Phe Leu Leu Glu Val Gln Ala Ala Val Pro Gly Leu Pro 770 780

Ser Arg Val Lys Cys Gly Ser Pro Gly Gln Leu Gln Gly His Ser Ile 785 790 795 800

Phe Ala Gln Asp Leu Arg Leu Cys Leu Asp Glu Thr Leu Ser Trp Asn 805 810 815

Cys Phe Gly Ile Ser Leu Leu Ala Met Ala Leu Gly Leu Val Val Pro 820 825 830

Met Leu His His Leu Cys Gly Trp Asp Leu Trp Tyr Cys Phe His Leu 835 840 845

Cys Leu Ala Trp Leu Pro His Arg Gly Gln Arg Arg Gly Ala Asp Ala 850 855 860

Leu Phe Tyr Asp Ala Phe Val Val Phe Asp Lys Ala Gln Ser Ala Val 865 870 880

.. .

Ala Asp Trp Val Tyr Asn Glu Leu Arg Val Gln Leu Glu Glu Arg Arg 885 890 895

Gly Arg Arg Ala Leu Arg Leu Cys Leu Glu Glu Arg Asp Trp Leu Pro 900 905 910

Gly Lys Thr Leu Phe Glu Asn Leu Trp Ala Ser Val Tyr Ser Ser Arg 915 920 925

Lys Thr Leu Phe Val Leu Ala His Thr Asp Arg Val Ser Gly Leu Leu 930 935 940

Arg Ala Ser Phe Leu Leu Ala Gln Gln Arg Leu Leu Glu Asp Arg Lys 955

Asp Val Val Val Leu Val Ile Leu Arg Pro Asp Ala Tyr Arg Ser Arg

Tyr Val Arg Leu Arg Gln Arg Leu Cys Arg Gln Ser Val Leu Leu Trp 985

Pro His Gln Pro Arg Gly Gln Gly Ser Phe Trp Ala Gln Leu Gly Thr

Ala Leu Thr Arg Asp Asn His His Phe Tyr Asn Arg Asn Phe Cys 1010 1015

Arg Gly Pro Thr Thr Ala Glu 1025 1030

<210> 6 <211> 819 <212> PRT

<213> Sus scrofa

<400> 6

Met Gly Pro Arg Cys Thr Leu His Pro Leu Ser Leu Leu Val Gln Val 10

Thr Ala Leu Ala Ala Leu Ala Gln Gly Arg Leu Pro Ala Phe Leu

Pro Cys Glu Leu Gln Pro His Gly Leu Val Asn Cys Asn Trp Leu Phe 40

Leu Lys Ser Val Pro His Phe Ser Ala Ala Ala Pro Arg Ala Asn Val 50 55

Thr Ser Leu Ser Leu Leu Ser Asn Arg Ile His His Leu His Asp Ser 75

Asp Phe Val His Leu Ser Ser Leu Arg Thr Leu Asn Leu Lys Trp Asn 85

Cys Pro Pro Ala Gly Leu Ser Pro Met His Phe Pro Cys His Met Thr 100 105

Ile Glu Pro Asn Thr Phe Leu Ala Val Pro Thr Leu Glu Glu Leu Asn 115 120 125

- Leu Ser Tyr Asn Ser Ile Thr Thr Val Pro Ala Leu Pro Asp Ser Leu 130 135 140
- Val Ser Leu Ser Leu Ser Arg Thr Asn Ile Leu Val Leu Asp Pro Thr 145 150 155 160
- His Leu Thr Gly Leu His Ala Leu Arg Tyr Leu Tyr Met Asp Gly Asn 165 170 175
- Cys Tyr Tyr Lys Asn Pro Cys Gln Gly Ala Leu Glu Val Val Pro Gly 180 185 190
- Ala Leu Leu Gly Leu Gly Asn Leu Thr His Leu Ser Leu Lys Tyr Asn 195 200 205
- Asn Leu Thr Glu Val Pro Arg Ser Leu Pro Pro Ser Leu Glu Thr Leu 210 215 220
- Leu Leu Ser Tyr Asn His Ile Val Thr Leu Thr Pro Glu Asp Leu Ala 225 230 235 240
- Asn Leu Thr Ala Leu Arg Val Leu Asp Val Gly Gly Asn Cys Arg Arg 245 250 255
- Cys Asp His Ala Arg Asn Pro Cys Arg Glu Cys Pro Lys Asp His Pro 260 265 270
- Lys Leu His Ser Asp Thr Phe Ser His Leu Ser Arg Leu Glu Gly Leu 275 280 285
- Val Leu Lys Asp Ser Ser Leu Tyr Asn Leu Asp Thr Arg Trp Phe Arg 290 295 300
- Gly Leu Asp Arg Leu Gln Val Leu Asp Leu Ser Glu Asn Phe Leu Tyr 305 310 315 320
- · Asp Cys Ile Thr Lys Thr Thr Ala Phe Gln Gly Leu Ala Arg Leu Arg 325 330 335
 - Ser Leu Asn Leu Ser Phe Asn Tyr His Lys Lys Val Ser Phe Ala His 340 345 350

Leu His Leu Ala Pro Ser Phe Gly His Leu Arg Ser Leu Lys Glu Leu 355 360 365

- Asp Met His Gly Ile Phe Phe Arg Ser Leu Ser Glu Thr Thr Leu Gln 370 375 380
- Pro Leu Val Gln Leu Pro Met Leu Gln Thr Leu Arg Leu Gln Met Asn 385 390 395 400
- Phe Ile Asn Gln Ala Gln Leu Ser Ile Phe Gly Ala Phe Pro Gly Leu
 405 410 415
- Leu Tyr Val Asp Leu Ser Asp Asn Arg Ile Ser Gly Ala Ala Arg Pro 420 425 430
- Val Ala Ile Thr Arg Glu Val Asp Gly Arg Glu Arg Val Trp Leu Pro 435 440 445
- Ser Arg Asn Leu Ala Pro Arg Pro Leu Asp Thr Leu Arg Ser Glu Asp 450 455 460
- Phe Met Pro Asn Cys Lys Ala Phe Ser Phe Thr Leu Asp Leu Ser Arg 480
- Asn Asn Leu Val Thr Ile Gln Ser Glu Met Phe Ala Arg Leu Ser Arg 485 490 495
- Leu Glu Cys Leu Arg Leu Ser His Asn Ser Ile Ser Gln Ala Val Asn 500 505 510
- Gly Ser Gln Phe Val Pro Leu Thr Ser Leu Arg Val Leu Asp Leu Ser 515 520 525
- His Asn Lys Leu Asp Leu Tyr His Gly Arg Ser Phe Thr Glu Leu Pro 530 535 540
- Arg Leu Glu Ala Leu Asp Leu Ser Tyr Asn Ser Gln Pro Phe Thr Met 545 550 555 560
- Gln Gly Val Gly His Asn Leu Ser Phe Val Ala Gln Leu Pro Ala Leu 565 570 575
- Arg Tyr Leu Ser Leu Ala His Asn Asp Ile His Ser Arg Val Ser Gln 580 585 585

Gln Leu Cys Ser Ala Ser Leu Cys Ala Leu Asp Phe Ser Gly Asn Asp 595 600 605

Leu Ser Arg Met Trp Ala Glu Gly Asp Leu Tyr Leu Arg Phe Phe Gln 610 620

Gly Leu Arg Ser Leu Val Trp Leu Asp Leu Ser Gln Asn His Leu His 625 630 635 640

Thr Leu Leu Pro Arg Ala Leu Asp Asn Leu Pro Lys Ser Leu Lys His
645 650 655

Leu His Leu Arg Asp Asn Asn Leu Ala Phe Phe Asn Trp Ser Ser Leu 660 665 670

Thr Leu Leu Pro Lys Leu Glu Thr Leu Asp Leu Ala Gly Asn Gln Leu 675 680 685

Lys Ala Leu Ser Asn Gly Ser Leu Pro Ser Gly Thr Gln Leu Arg Arg 690 695 700

Leu Asp Leu Ser Gly Asn Ser Ile Gly Phe Val Asn Pro Gly Phe Phe 705 710 715 720

Ala Leu Ala Lys Gln Leu Glu Glu Leu Asn Leu Ser Ala Asn Ala Leu 725 730 735

Lys Thr Val Glu Pro Ser Trp Phe Gly Ser Met Val Gly Asn Leu Lys 740 745 750

Val Leu Asp Val Ser Ala Asn Pro Leu His Cys Ala Cys Gly Ala Thr 755 760 765

Phe Val Gly Phe Leu Leu Glu Val Gln Ala Ala Val Pro Gly Leu Pro 770 775 780

Ser Arg Val Lys Cys Gly Ser Pro Gly Gln Leu Gln Gly His Ser Ile 785 790 795 800

Phe Ala Gln Asp Leu Arg Leu Cys Leu Asp Glu Thr Leu Ser Trp Asn 805 810 815

Cys Phe Gly

<210> 7
<211> 3352
<212> DNA
<213> Sus scrofa

<400> 7 gagcacgaac atcettcact gtagctgctg cccggtctgc cagccagacc ctttggagaa 60 gaccccactc cctgtcatgg gcccccgctg caccctgcac cccctttctc tcctggtgca 120 ggtgacagcg ctggctgcgg ctctggccca gggcaggctg cctgccttcc tgccctgtga 180 gctccagccc cacggcctgg tgaactgcaa ctggctcttc ctgaagtccg tgccccactt 240 ctcggcggca gcgccccggg ccaacgtcac cagcctctcc ttactctcca accgcatcca 300 ccacctgcac gactccgact tcgtccacct gtccagccta cgaactctca acctcaagtg 360 gaactgcccg ccggctggcc tcagccccat gcacttcccc tgccacatga ccatcgagcc 420 caacacette etggeegtge ccaecetgga ggagetgaac etgagetaca acageateae 480 gaccgtgcct gccctgcccg actccctcgt gtccctgtcg ctgagccgca ccaacatcct 540 ggtgctagac cccacccacc tcactggcct acatgccctg cgctacctgt acatggatgg 600 caactgctac tacaagaacc cctgccaggg ggcgctggag gtggtgccgg gtgccctcct 660 cggcctgggc aacctcacac atctctcact caagtacaac aatctcacgg aggtgccccg 720 cagcetgeec eccageetgg agaceetget gttgteetac aaccacattg teaccetgae 780 gcctgaggac ctggccaatc tgactgccct gcgcgtgctt gatgtggggg ggaactgccg 840 ccgctgtgac catgcccgca acccctgcag ggagtgccca aaggaccacc ccaagctgca 900 ctctgacacc ttcagccacc tgagccgcct cgaaggcctg gtgttgaaag acagttctct 960 ctacaacctg gacaccaggt ggttccgagg cctggacagg ctccaagtgc tggacctgag 1020 tgagaacttc ctctacgact gcatcaccaa gaccacggcc ttccagggcc tggcccgact 1080 gcgcagcctc aacctgtcct tcaattacca caagaaggtg tcctttgccc acctgcacct 1140 ggcaccetee titgggcace teeggteeet gaaggagetg gacatgcatg geatettett 1200 ccgctcgctc agtgagacca cgctccaacc tctggtccaa ctgcctatgc tccagaccct 1260 gegeetgeag atgaacttea ttaaccagge ecageteage atetttgggg cettecetgg 1320 cctgctgtac gtggacctat cggacaaccg catcagcgga gctgcaaggc cagtggccat 1380 tactagggag gtggatggta gggagagggt ctggctgcct tccaggaacc tcgctccacg 1440 tccactggac actctccgct cagaggactt catgccaaac tgcaaggcct tcagcttcac 1500

cttggacctg tctcggaaca acctggtgac aatccagtcg gagatgtttg ctcgcctctc 1560 acgcctcgag tgcctgcgcc tgagccacaa cagcatctcc caggcggtca atggctctca 1620 gtttgtgccg ctgaccagcc tgcgggtgct ggacctgtcc cacaacaagc tggacctgta 1680 tcacgggcgc tcgttcacgg agctgccgcg cctggaagca ctggacctca gctacaatag 1740 ccagccettt accatgcagg gtgtgggcca caacctcage ttcgtggccc agetgcccgc 1800 cctgcgctac ctcagcctgg cgcacaatga catccatagc cgagtgtccc agcagctctg 1860 tagogoctca ctgtgcgccc tggactttag cggcaacgat ctgagccgga tgtgggctga 1920 1980 gggagacete tateteeget tetteeaagg cetaagaage etagtetgge tggacetgte ccagaaccac ctgcacaccc tcctgccacg tgccctggac aacctcccca aaagcctgaa 2040 gcatctgcat ctccgtgaca ataacctggc cttcttcaac tggagcagcc tgaccctcct 2100 gcccaagetg gaaaccetgg acttggctgg aaaccagetg aaggccctaa gcaatggcag 2160 cctgccatct ggcacccagc tgcggaggct ggacctcagt ggcaacagca tcggctttgt 2220 qaaccctggc ttctttgccc tggccaagca gttagaagag ctcaacctca gcgccaatgc 2280 cctcaagaca gtggagccct cctggtttgg ctcgatggtg ggcaacctga aagtcctaga 2340 cgtgagcgcc aaccetetge actgtgcetg tggggcgacc ttcgtggget teetgetgga 2400 ggtacaggct gccgtgcctg ggctgcccag ccgcgtcaag tgtggcagtc cggggcagct 2460 2520 ccagggccat ageatetttg egeaagaeet gegeetetge etggatgaga eeetetegtg gaactgtttt ggcatctege tgetggeeat ggceetggge etggttgtge ceatgetgea 2580 2640 ccacctetge ggetgggace tetggtactg ettecacetg tgcctggcet ggetgececa ccgagggcag cggcggggcg cagacgccct gttctatgat gccttcgtgg tctttgacaa 2700 2760 agctcagagt gctgtggccg actgggtgta caacgagctg cgggtgcagc tggaggagcg ccgtgggcgc cgcgcactgc gcctgtgcct ggaggagcga gactggttac ctggcaagac 2820 gctcttcgag aacctgtggg cctcagtcta cagcagccgc aagaccctgt ttgtgctggc 2880 ccacacggac cgtgtcagcg gcctcttgcg tgccagtttc ctgctggccc agcagcgcct 2940 gctggaggac cgcaaggacg ttgtagtgct ggtgatcctg cgccccgatg cctaccgctc 3000 ecgetacgtg eggetgegee agegeetetg eegecagagt gteeteetet ggeeecacea 3060 gccccgtggg cagggcagct tctgggccca gctgggcaca gccctgacca gggacaacca 3120 ccacttctat aaccggaact tctgccgqqg ccccacgaca gccgaatagc actgagtgac 3180 agcccagttg ccccagcccc cctggatttg cctctctgcc tggggtgccc caacctgctt 3240 3300 . tgctcagcca caccactgct ctgctccctg ttccccaccc caccccccag cctggcatgt

aacatgtgcc caataaatgc taccggaggg ccaagaaaaa aaaaaaaaaa	3352
<210> 8 <211> 2457 <212> DNA <213> Sus scrofa	
<400> 8	
atgggccccc gctgcaccct gcaccccctt tctctcctgg tgcaggtgac agcgctggct	60
geggetetgg cecagggeag getgeetgee tteetgeeet gtgageteea geeeeaegge	120
ctggtgaact gcaactggct cttcctgaag teegtgeece acttctegge ggcagegeec	180
cgggccaacg teaccageet etecttaete tecaacegea tecaccaeet geacgaetee	240
gacttegtee acctgtecag cetacgaact etcaacetea agtggaactg eeegeegget	300
ggcctcagcc ccatgcactt cccctgccac atgaccatcg agcccaacac cttcctggcc	360
gtgcccaccc tggaggagct gaacctgagc tacaacagca tcacgaccgt gcctgccctg	420
cccgactccc tcgtgtccct gtcgctgagc cgcaccaaca tcctggtgct agaccccacc	480
cacctcactg gcctacatgc cctgcgctac ctgtacatgg atggcaactg ctactacaag	540
aacccctgcc agggggcgct ggaggtggtg ccgggtgccc tcctcggcct gggcaacctc	600
acacatetet caeteaagta caacaatete aeggaggtge eeegeageet geeeceeage	660
ctggagaccc tgctgttgtc ctacaaccac attgtcaccc tgacgcctga ggacctggcc	720
aatetgaetg ceetgegegt gettgatgtg ggggggaaet geegeegetg tgaccatgee	780
cgcaacccct gcagggagtg cccaaaggac caccccaagc tgcactctga caccttcagc	840
cacctgagcc gcctcgaagg cctggtgttg aaagacagtt ctctctacaa cctggacacc	900
aggtggttcc gaggcctgga caggctccaa gtgctggacc tgagtgagaa cttcctctac	960
gactgcatca ccaagaccac ggccttccag ggcctggccc gactgcgcag cctcaacctg	1020
teetteaatt accaeaagaa ggtgteettt geeeacetge acctggeace eteetttggg	1080
cacctccggt ccctgaagga gctggacatg catggcatct tcttccgctc gctcagtgag	1140
accacgetee aacetetggt ccaactgeet atgetecaga ccetgegeet gcagatgaac	1200
ttcattaacc aggcccagct cagcatcttt ggggccttcc ctggcctgct gtacgtggac	1260
ctatcggaca accgcatcag cggagctgca aggccagtgg ccattactag ggaggtggat	
ggtagggaga gggtctggct gccttccagg aacctcgctc cacgtccact ggacactctc	1320
cgctcagagg acttcatgcc aaactgcaag gccttcagct tcaccttgga cctgtctcgg	1380
aacaacctgg tgacaatcca gtcggagatg tttgctcgcc tctcacgcct cgagtgcctg	1440
-5 -5 3003349409 titlgctcgcc tctcacgcct cgagtgcctg	1500

cgcctgagcc	acaacagcat	ctcccaggcg	gtcaatggct	ctcagtttgt	gccgctgacc	1560
agcctgcggg	tgctggacct	gtcccacaac	aagctggacc	tgtatcacgg	gcgctcgttc	1620
acggagctgc	cgcgcctgga	agcactggac	ctcagctaca	atagccagcc	ctttaccatg	1680
cagggtgtgg	gccacaacct	cagcttcgtg	gcccagctgc	ccgccctgcg	ctacctcagc	1740
ctggcgcaca	atgacatcca	tagccgagtg	tcccagcagc	tctgtagcgc	ctcactgtgc	1800
gccctggact	ttagcggcaa	cgatctgagc	cggatgtggg	ctgagggaga	cctctatctc	1860
cgcttcttcc	aaggcctaag	aagcctagtc	tggctggacc	tgtcccagaa	ccacctgcac	1920
accetectge	cacgtgccct	ggacaacctc	cccaaaagcc	tgaagcatct	gcatctccgt	1980
gacaataacc	tggccttctt	caactggagc	agcctgaccc	tectgeccaa	gctggaaacc	2040
ctggacttgg	ctggaaacca	gctgaaggcc	ctaagcaatg	gcagcctgcc	atctggcacc	2100
cagctgcgga	ggctggacct	cagtggcaac	agcatcggct	ttgtgaaccc	tggcttcttt	2160
gccctggcca	agcagttaga	agagctcaac	ctcagcgcca	atgccctcaa	gacagtggag	2220
ccctcctggt	ttggctcgat	ggtgggcaac	ctgaaagtcc	tagacgtgag	cgccaaccct	2280
ctgcactgtg	cctgtggggc	gaccttcgtg	ggcttcctgc	tggaggtaca	ggctgccgtg	2340
cctgggctgc	ccagccgcgt	caagtgtggc	agtccggggc	agctccaggg	ccatagcatc	2400
tttgcgcaag	acctgcgcct	ctgcctggat	gagaccctct	cgtggaactg	ttttggc	2457

<210> 9
<211> 1029
<212> PRT
<213> Bos taurus

<400> 9

Met Gly Pro Tyr Cys Ala Pro His Pro Leu Ser Leu Leu Val Gln Ala

Ala Ala Leu Ala Ala Leu Ala Glu Gly Thr Leu Pro Ala Phe Leu 25

Pro Cys Glu Leu Gln Pro His Gly Gln Val Asp Cys Asn Trp Leu Phe - 40

Leu Lys Ser Val Pro His Phe Ser Ala Gly Ala Pro Arg Ala Asn Val ...55

Thr Ser Leu Ser Leu Ile Ser Asn Arg Ile His His Leu His Asp Ser 70

Asp Phe Val His Leu Ser Asn Leu Arg Val Leu Asn Leu Lys Trp Asn 85 90 95

- Cys Pro Pro Ala Gly Leu Ser Pro Met His Phe Pro Cys Arg Met Thr 100 105 110
- Ile Glu Pro Asn Thr Phe Leu Ala Val Pro Thr Leu Glu Glu Leu Asn 115 120 125
- Leu Ser Tyr Asn Gly Ile Thr Thr Val Pro Ala Leu Pro Ser Ser Leu 130 135 140
- Val Ser Leu Ser Leu Ser His Thr Ser Ile Leu Val Leu Gly Pro Thr 145 150 155 160
- His Phe Thr Gly Leu His Ala Leu Arg Phe Leu Tyr Met Asp Gly Asn 165 170 175
- Cys Tyr Tyr Met Asn Pro Cys Pro Arg Ala Leu Glu Val Ala Pro Gly
 180 185 190
- Ala Leu Leu Gly Leu Gly Asn Leu Thr His Leu Ser Leu Lys Tyr Asn 195 200 205
- Asn Leu Thr Glu Val Pro Arg Arg Leu Pro Pro Ser Leu Asp Thr Leu 210 215 220
- Leu Leu Ser Tyr Asn His Ile Val Thr Leu Ala Pro Glu Asp Leu Ala 225 230 235 240
- Asn Leu Thr Ala Leu Arg Val Leu Asp Val Gly Gly Asn Cys Arg Arg 245 250 255
- Cys Asp His Ala Arg Asn Pro Cys Arg Glu Cys Pro Lys Asn Phe Pro 260 265 , 270
- Lys Leu His Pro Asp Thr Phe Ser His Leu Ser Arg Leu Glu Gly Leu 275 280 285
- Val Leu Lys Asp Ser Ser Leu Tyr Lys Leu Glu Lys Asp Trp Phe Arg 290 295 300
- Gly Leu Gly Arg Leu Gln Val Leu Asp Leu Ser Glu Asn Phe Leu Tyr

305 310 315 320

Asp Tyr Ile Thr Lys Thr Thr Ile Phe Asn Asp Leu Thr Gln Leu Arg 325 330 335

Arg Leu Asn Leu Ser Phe Asn Tyr His Lys Lys Val Ser Phe Ala His 340 345 350

Leu His Leu Ala Ser Ser Phe Gly Ser Leu Val Ser Leu Glu Lys Leu 355 360 365

Asp Met His Gly Ile Phe Phe Arg Ser Leu Thr Asn Ile Thr Leu Gln 370 380

Ser Leu Thr Arg Leu Pro Lys Leu Gln Ser Leu His Leu Gln Leu Asn 385 390 395 400

Phe Ile Asn Gln Ala Gln Leu Ser Ile Phe Gly Ala Phe Pro Ser Leu 405 410 415

Leu Phe Val Asp Leu Ser Asp Asn Arg Ile Ser Gly Ala Ala Thr Pro 420 425 430

Ala Ala Leu Gly Glu Val Asp Ser Arg Val Glu Val Trp Arg Leu
435 440 445

Pro Arg Gly Leu Ala Pro Gly Pro Leu Asp Ala Val Ser Ser Lys Asp 450 450

Phe Met Pro Ser Cys Asn Leu Asn Phe Thr Leu Asp Leu Ser Arg Asn 465 470 475 480

Asn Leu Val Thr Ile Gln Gln Glu Met Phe Thr Arg Leu Ser Arg Leu 485 490 495

Gln Cys Leu Arg Leu Ser His Asn Ser Ile Ser Gln Ala Val Asn Gly 500 505 510

Ser Gln Phe Val Pro Leu Thr Ser Leu Arg Val Leu Asp Leu Ser His 515 520 525

Asn Lys Leu Asp Leu Tyr His Gly Arg Ser Phe Thr Glu Leu Pro Gln 530 540

Leu Glu Ala Leu Asp Leu Ser Tyr Asn Ser Gln Pro Phe Ser Met Gln 545 550 560

- Gly Val Gly His Asn Leu Ser Phe Val Ala Gln Leu Pro Ser Leu Arg 565 570 575
- Tyr Leu Ser Leu Ala His Asn Gly Ile His Ser Arg Val Ser Gln Lys 580 585 590
- Leu Ser Ser Ala Ser Leu Arg Ala Leu Asp Phe Ser Gly Asn Ser Leu 595 600 605
- Ser Gln Met Trp Ala Glu Gly Asp Leu Tyr Leu Cys Phe Phe Lys Gly 610 620
- Leu Arg Asn Leu Val Gln Leu Asp Leu Ser Glu Asn His Leu His Thr 625 630 635 640
- Leu Leu Pro Arg His Leu Asp Asn Leu Pro Lys Ser Leu Arg Gln Leu 645 650 655
- Arg Leu Arg Asp Asn Asn Leu Ala Phe Phe Asn Trp Ser Ser Leu Thr 660 665 670
- Val Leu Pro Arg Leu Glu Ala Leu Asp Leu Ala Gly Asn Gln Leu Lys 675 680 685
- Ala Leu Ser Asn Gly Ser Leu Pro Pro Gly Ile Arg Leu Gln Lys Leu 690 695 700
- Asp Val Ser Ser Asn Ser Ile Gly Phe Val Ile Pro Gly Phe Phe Val 705 710 715 720
- Arg Ala Thr Arg Leu Ile Glu Leu Asn Leu Ser Ala Asn Ala Leu Lys 725 730 735
- Thr Val Asp Pro Ser Trp Phe Gly Ser Leu Ala Gly Thr Leu Lys Ile 740 745 750
- Leu Asp Val Ser Ala Asn Pro Leu His Cys Ala Cys Gly Ala Ala Phe
 755 760 765
- Val Asp Phe Leu Leu Glu Arg Gln Glu Ala Val Pro Gly Leu Ser Arg 770 775 780

Arg Val Thr Cys Gly Ser Pro Gly Gln Leu Gln Gly Arg Ser Ile Phe 785 790 795 800

- Thr Gln Asp Leu Arg Leu Cys Leu Asp Glu Thr Leu Ser Leu Asp Cys 805 810 815
- Phe Gly Leu Ser Leu Leu Met Val Ala Leu Gly Leu Ala Val Pro Met 820 825 830
- Leu His His Leu Cys Gly Trp Asp Leu Trp Tyr Cys Phe His Leu Cys 835 840 845
- Leu Ala His Leu Pro Arg Arg Arg Gln Arg Gly Glu Asp Thr Leu 850 855 860
- Leu Tyr Asp Ala Val Val Phe Asp Lys Val Gln Ser Ala Val Ala 865 870 875 880
- Asp Trp Val Tyr Asn Glu Leu Arg Val Gln Leu Glu Glu Arg Arg Gly 885 890 895
- Arg Arg Ala Leu Arg Leu Cys Leu Glu Glu Arg Asp Trp Leu Pro Gly 900 905 910
- Lys Thr Leu Phe Glu Asn Leu Trp Ala Ser Val Tyr Ser Ser Arg Lys 915 920 925
- Thr Met Phe Val Leu Asp His Thr Asp Arg Val Ser Gly Leu Leu Arg 930 935 940

, :

- Ala Ser Phe Leu Leu Ala Gln Gln Arg Leu Leu Glu Asp Arg Lys Asp 945 950 955 960
- Val Val Leu Val Ile Leu Arg Pro Ala Ala Tyr Arg Ser Arg Tyr 965 970 975
- Val Arg Leu Arg Gln Arg Leu Cys Arg Gln Ser Val Leu Leu Trp Pro 980 985 990
- His Gln Pro Ser Gly Gln Gly Ser Phe Trp Ala Asn Leu Gly Ile Ala 995 1000 1005
- Leu Thr Arg Asp Asn Arg His Phe Tyr Asn Arg Asn Phe Cys Arg 1010 1015 1020

Gly Pro Thr Thr Ala Glu 1025

<210> 10

<211> 818

<212> PRT

<213> Bos taurus

<400> 10

Met Gly Pro Tyr Cys Ala Pro His Pro Leu Ser Leu Leu Val Gln Ala 1 5 10 10 15

Ala Ala Leu Ala Ala Leu Ala Glu Gly Thr Leu Pro Ala Phe Leu 20 25 30

Pro Cys Glu Leu Gln Pro His Gly Gln Val Asp Cys Asn Trp Leu Phe 35 40 45

Leu Lys Ser Val Pro His Phe Ser Ala Gly Ala Pro Arg Ala Asn Val

Thr Ser Leu Ser Leu Ile Ser Asn Arg Ile His His Leu His Asp Ser 70 75 80

Asp Phe Val His Leu Ser Asn Leu Arg Val Leu Asn Leu Lys Trp Asn 85 90 95

Cys Pro Pro Ala Gly Leu Ser Pro Met His Phe Pro Cys Arg Met Thr 100 105 110

Ile Glu Pro Asn Thr Phe Leu Ala Val Pro Thr Leu Glu Glu Leu Asn 115 120 125 .

Leu Ser Tyr Asn Gly Ile Thr Thr Val Pro Ala Leu Pro Ser Ser Leu 130 135 140

Val Ser Leu Ser Leu Ser His Thr Ser Ile Leu Val Leu Gly Pro Thr 145 150 155 160

His Phe Thr Gly Leu His Ala Leu Arg Phe Leu Tyr Met Asp Gly Asn 165 170 175

Cys Tyr Tyr Met Asn Pro Cys Pro Arg Ala Leu Glu Val Ala Pro Gly 180 185 190

Ala Leu Leu Gly Leu Gly Asn Leu Thr His Leu Ser Leu Lys Tyr Asn 195 200 205

Asn Leu Thr Glu Val Pro Arg Arg Leu Pro Pro Ser Leu Asp Thr Leu 210 215 220

Leu Leu Ser Tyr Asn His Ile Val Thr Leu Ala Pro Glu Asp Leu Ala 225 230 235 240

Asn Leu Thr Ala Leu Arg Val Leu Asp Val Gly Gly Asn Cys Arg Arg 245 250 255

Cys Asp His Ala Arg Asn Pro Cys Arg Glu Cys Pro Lys Asn Phe Pro 260 265 270

Lys Leu His Pro Asp Thr Phe Ser His Leu Ser Arg Leu Glu Gly Leu 275 280 285

Val Leu Lys Asp Ser Ser Leu Tyr Lys Leu Glu Lys Asp Trp Phe Arg 290 295 300

Gly Leu Gly Arg Leu Gln Val Leu Asp Leu Ser Glu Asn Phe Leu Tyr 305 310 315 320

Asp Tyr Ile Thr Lys Thr Thr Ile Phe Asn Asp Leu Thr Gln Leu Arg 325 330 335

Arg Leu Asn Leu Ser Phe Asn Tyr His Lys Lys Val Ser Phe Ala His 340 345 350

Leu His Leu Ala Ser Ser Phe Gly Ser Leu Val Ser Leu Glu Lys Leu 355 360 365

Asp Met His Gly Ile Phe Phe Arg Ser Leu Thr Asn Ile Thr Leu Gln 370 375 380

Ser Leu Thr Arg Leu Pro Lys Leu Gln Ser Leu His Leu Gln Leu Asn 385 390 395 400

Phe Ile Asn Gln Ala Gln Leu Ser Ile Phe Gly Ala Phe Pro Ser Leu 405 410 415

Leu Phe Val Asp Leu Ser Asp Asn Arg Ile Ser Gly Ala Ala Thr Pro

420 425 430

Ala Ala Leu Gly Glu Val Asp Ser Arg Val Glu Val Trp Arg Leu
435 440 445

Pro Arg Gly Leu Ala Pro Gly Pro Leu Asp Ala Val Ser Ser Lys Asp 450 455

Phe Met Pro Ser Cys Asn Leu Asn Phe Thr Leu Asp Leu Ser Arg Asn 465 470 475 480

Asn Leu Val Thr Ile Gln Gln Glu Met Phe Thr Arg Leu Ser Arg Leu 485 490 495

Gln Cys Leu Arg Leu Ser His Asn Ser Ile Ser Gln Ala Val Asn Gly
500 505 510

Ser Gln Phe Val Pro Leu Thr Ser Leu Arg Val Leu Asp Leu Ser His 515 520 525

Asn Lys Leu Asp Leu Tyr His Gly Arg Ser Phe Thr Glu Leu Pro Gln 530 540

Leu Glu Ala Leu Asp Leu Ser Tyr Asn Ser Gln Pro Phe Ser Met Gln 545 550 555 560

Gly Val Gly His Asn Leu Ser Phe Val Ala Gln Leu Pro Ser Leu Arg 565 570 575

Tyr Leu Ser Leu Ala His Asn Gly Ile His Ser Arg Val Ser Gln Lys 580 585 590

Leu Ser Ser Ala Ser Leu Arg Ala Leu Asp Phe Ser Gly Asn Ser Leu 595 600 605

Ser Gln Met Trp Ala Glu Gly Asp Leu Tyr Leu Cys Phe Phe Lys Gly 610 620

Leu Arg Asn Leu Val Gln Leu Asp Leu Ser Glu Asn His Leu His Thr 625 630 630 635

Leu Leu Pro Arg His Leu Asp Asn Leu Pro Lys Ser Leu Arg Gln Leu 645 650 655

Arg Leu Arg Asp Asn Asn Leu Ala Phe Phe Asn Trp Ser Ser Leu Thr 660 Val Leu Pro Arg Leu Glu Ala Leu Asp Leu Ala Gly Asn Gln Leu Lys Ala Leu Ser Asn Gly Ser Leu Pro Pro Gly Ile Arg Leu Gln Lys Leu 690 Asp Val Ser Ser Asn Ser Ile Gly Phe Val Ile Pro Gly Phe Phe Val 705 710 Arg Ala Thr Arg Leu Ile Glu Leu Asn Leu Ser Ala Asn Ala Leu Lys 725 730 Thr Val Asp Pro Ser Trp Phe Gly Ser Leu Ala Gly Thr Leu Lys Ile 750 Leu Asp Val Ser Ala Asn Pro Leu His Cys Ala Cys Gly Ala Ala Phe 755 765 Val Asp Phe Leu Leu Glu Arg Gln Glu Ala Val Pro Gly Leu Ser Arg 770 775 Arg Val Thr Cys Gly Ser Pro Gly Gln Leu Gln Gly Arg Ser Ile Phe 785 790 Thr Gln Asp Leu Arg Leu Cys Leu Asp Glu Thr Leu Ser Leu Asp Cys 805 Phe Gly <210> 11 <211> 3191 <212> DNA <213> Bos taurus <400> 11 gggaagtggg cgccaagcat ccttccctgc agctgcctcc caacctgccc gccagaccct 60 ctggagaagc cgcattccct gtcatgggcc cctactgtgc cccgcacccc ctttctctcc 120 . tggtgcaggc ggcggcactg gcagcggccc tggccgaggg caccctgcct gccttcctgc 180 cetgtgaget ceagececat ggteaggtgg actgeaactg getgtteetg aagtetgtge 240 cgcacttttc ggctggagcc ccccgggcca atgtcaccag cctctcctta atctccaacc 300

gcatccacca cttgcatgac	tctgacttcg	tccacctgtc	caacctgcgg	gtcctcaacc	360
tcaagtggaa ctgcccgccg	gccggcctca	gccccatgca	cttcccctgc	cgtatgacca	420
tcgagcccaa caccttcctg	gctgtgccca	ccctggagga	gctgaacctg	agctacaacg	480
gcatcacgac cgtgcctgcc	ctgcccagtt	ccctcgtgtc	cctgtcgctg	agccacacca	540
gcatcctggt gctaggcccc	acccacttca	ccggcctgca	cgccctgcgc	tttctgtaca	600
tggacggcaa ctgctactac	atgaacccct	gcccgcgggc	cctggaggtg	gccccaggcg	660
ccctcctcgg cctgggcaac	ctcacgcacc	tgtcgctcaa	gtacaacaac	ctcacggagg	720
tgccccgccg cctgccccc	agcctggaca	ccctgctgct	gtcctacaac	cacattgtca	780
ccctggcacc cgaggacctg	gccaacctga	ctgccctgcg	cgtgcttgac	gtgggtggga	840
actgeegeeg etgegaeeat	gcccgcaacc	cctgcaggga	gtgcccaaag	aacttcccca	900
agctgcaccc tgacaccttc	agtcacctga	gccgcctcga	aggcctggtg	ttgaaggaca	960
gttctctcta caaactagag	aaagattggt	tccgcggcct	gggcaggctc	caagtgctcg	1020
acctgagtga gaacttcctc	tatgactaca	tcaccaagac	caccatcttc	aacgacctga	1080
cccagctgcg cagactcaac	ctgtccttca	attaccacaa	gaaggtgtcc	ttcgcccacc	1140
tgcacctage gtcctccttt	gggagtctgg	tgtccctgga	gaagctggac	atgcacggca	1200
tcttcttccg ctccctcacc	aacatcacgc	tccagtcgct	gacccggctg	cccaagctcc	1260
agagtctgca tctgcagctg	aacttcatca	accaggccca	gctcagcatc	tttggggcct	1320
tecegageet getettegtg	gacctgtcgg	acaaccgcat	cagcggagcc	gcgacgccag	1380
cggccgccct gggggaggtg	gacagcaggg	tggaagtetg	gcgattgccc	aggggcctcg	1440
ctccaggccc gctggacgcc	gtcagctcaa	aggacttcat	gccaagctgc	aacctcaact	1500
tcaccttgga cctgtcacgg	aacaacctgg	tgacaatcca	gcaagagatg	tttacccgcc	1560
totocogoot coagtgootg	cgcctgagcc	acaacagcat	ctcgcaggcg	gttaatggct	1620
cccagttcgt gccgctgacc	agcctgcgag	tgctcgacct	gtcccacaac	aagctggacc	1680
tgtaccatgg gcgctcattc	acggagctgc	cgcagctgga	ggcactggac	ctcagctaca	1740
acagecagee etteageatg	cagggcgtgg	gccacaacct	cagcttcgtg	gcccagctgc	1800
cctccctgcg ctacctcagc	cttgcgcaca	atggcatcca	cagccgcgtg	tcacagaagc	1860
tcagcagcgc ctcgttgcgc	gccctggact	tcagcggcaa	ctccctgagc	cagatgtggg	1920
ccgagggaga cctctatctc	tgctttttca	aaggcttgag	gaacctggtc	cagctggacc	1980
tgtccgagaa ccatctgcac	accetectge	ctcgtcacct	ggacaacctg	cccaagagcc	2040

tgcggcagct	gcgtctccgg	gacaataacc	tggccttctt	caactggagc	agcctgaccg	2100
tcctgccccg	gctggaagcc	ctggatctgg	caggaaacca	gctgaaggcc	ctgagcaacg	2160
gcagcctgcc	gcctggcatc	cggctccaga	agctggacgt	gagcagcaac	agcatcggct	2220
tegtgatece	cggcttcttc	gtccgcgcga	ctcggctgat	agagcttaac	ctcagcgcca	2280
atgccctgaa	gacagtggat	ccctcctggt	teggtteett	agcagggacc	ctgaaaatcc	2340
tagacgtgag	cgccaacccg	ctccactgcg	cetgcggggc	ggcctttgtg	gacttcctgc	2400
tggagagaca	ggaggccgtg	cccgggctgt	ccaggcgcgt	cacatgtggc	agtccgggcc	2460
agctccaggg	ccgcagcatc	ttcacacagg	acctgcgcct	ctgcctggat	gagaccctct	2520
ccttggactg	ctttggcctc	tcactgctaa	tggtggcgct	gggcctggca	gtgcccatgc	2580
tgcaccacct	ctgtggctgg	gacctctggt	actgcttcca	cctgtgtctg	gcccatttgc	2640
cccgacggcg	gcggcagcgg	ggcgaggaca	ccctgctcta	tgatgccgtc	gtggtcttcg	2700
acaaggtgca	gagtgcagtg	gctgattggg	tgtacaacga	gctccgcgtg	cagctggagg	2760
agcgccgggg	gcgccgggcg	ctccgcctct	gcctggagga	gcgagactgg	ctccctggta	2820
agacgctctt	cgagaacctg	tgggcctcgg	tctacagcag	ccgcaagacc	atgttcgtgc	2880
tggaccacac	ggaccgggtc	agcggcctcc	tgcgcgccag	cttcctgctg	geccageage	2940
gcctgttgga	ggaccgcaag	gacgtcgtag	tgctggtgat	cctgcgcccc	gccgcctatc	3000
ggtcccgcta	cgtgcggctg	cgccagcgcc	tetgeegeea	gagcgtcctc	ctctggcccc	3060
accagcccag	tggccagggt	agtttctggg	ccaacctggg	catagccctg	accagggaca	3120
accgtcactt	ctataaccgg	aacttctgcc	ggggccccac	gacagccgaa	tagcacagag	3180
tgactgccca	g					3191
<210> 12						

<211> 2454

<212> DNA

<213> Bos taurus

<400> 12

atgggccct actgtgccc gcacccctt tctctctgg tgcaggggg ggcactggca 60 gcggccctgg ccgagggca cctgcctgcc ttcctgcct gtgagctcca gccccatggt 120 caggtggact gcaactggct gttcctgaag tctgtgccgc acttttcggc tggagccccc 180 cgggccaatg tcaccagcct ctccttaatc tccaaccgca tccaccactt gcatgactct 240 gacttcgtcc acctgtccaa cctgcggtc ctcaacctca agtggaactg cccgccggcc 300 ggcctcagcc ccatgcactt cccctgccgt atgaccatcg agcccaacac cttcctggct 360

gtgcccaccc	tggaggagct	gaacctgagc	tacaacggca	tcacgaccgt	geetgeeetg	420
cccagttccc	tegtgteeet	gtcgctgagc	cacaccagca	tectggtget	aggccccacc	480
cacttcaccg	gcctgcacgc	cctgcgcttt	ctgtacatgg	acggcaactg	ctactacatg	540
aacccctgcc	cgcgggccct	ggaggtggcc	ccaggcgccc	tcctcggcct	gggcaacctc	600
acgcacctgt	cgctcaagta	caacaacctc	acggaggtgc	cccgccgcct	gcccccagc	660
ctggacaccc	tgctgctgtc	ctacaaccac	attgtcaccc	tggcacccga	ggacctggcc	720
aacctgactg	ccctgcgcgt	gcttgacgtg	ggtgggaact	gccgccgctg	cgaccatgcc	780
cgcaacccct	gcagggagtg	cccaaagaac	ttccccaagc	tgcaccctga	caccttcagt	840
cacctgagcc	gcctcgaagg	cctggtgttg	aaggacagtt	ctctctacaa	actagagaaa	900
gattggttcc	gcggcctggg	caggctccaa	gtgctcgacc	tgagtgagaa	cttcctctat	960
gactacatca	ccaagaccac	catcttcaac	gacctgaccc	agctgcgcag	actcaacctg	1020
tccttcaatt	accacaagaa	ggtgtccttc	gcccacctgc	acctagcgtc	ctcctttggg	1080
agtctggtgt	ccctggagaa	gctggacatg	cacggcatct	tetteegete	cctcaccaac	1140
atcacgetee	agtcgctgac	ceggetgece	aagctccaga	gtctgcatct	gcagctgaac	1200
ttcatcaacc	aggcccagct	cagcatcttt	ggggccttcc	cgagcctgct	cttcgtggac	1260
ctgtcggaca	accgcatcag	cggagccgcg	acgccagcgg	ccgccctggg	ggaggtggac	1320
agcagggtgg	aagtctggcg	attgcccagg	ggcctcgctc	caggcccgct	ggacgccgtc	1380
agctcaaagg	acttcatgcc	aagctgcaac	ctcaacttca	ccttggacct	gtcacggaac	1440
aacctggtga	caatccagca	agagatgttt	accegeetet	cccgcctcca	gtgcctgcgc	1500
ctgagccaca	acagcatctc	gcaggcggtt	aatggctccc	agttcgtgcc	gctgaccagc	1560
ctgcgagtgc	tcgacctgtc	ccacaacaag	ctggacctgt	accatgggcg	ctcattcacg	1620
gagctgccgc	agctggaggc	actggacete	agctacaaca	gccagccctt	cagcatgcag	1680
ggcgtgggcc	acaacctcag	cttcgtggcc	cagctgccct	ccctgcgcta	cctcagcctt	1740
gcgcacaatg	gcatccacag	ccgcgtgtca	cagaagctca	gcagcgcctc	gttgcgcgcc	1800
ctggacttca	gcggcaactc	cctgagccag	atgtgggccg	agggagacct	ctatctctgc	1860
tttttcaaag	gcttgaggaa	cctggtccag	ctggacctgt	ccgagaacca	tctgcacacc	1920
ctcctgcctc	gtcacctgga	caacctgccc	aagagcctgc	ggcagctgcg	tctccgggac	1980
aataacctgg	ccttcttcaa	ctggagcagc	ctgaccgtcc	tgccccggct	ggaagccctg	2040
gatctggcag	gaaaccagct	gaaggccctg	agcaacggca	gcctgccgcc	tggcatccgg	2100
ctccagaagc	tggacgtgag	cagcaacagc	atcggcttcg	tgatccccgg	ettettegte	2160

cgcgcgactc ggctgataga gcttaacetc agcgccaatg ccctgaagac agtggatccc 2220
tcctggttcg gttccttagc agggaccetg aaaatcctag acgtgagcgc caacccgctc 2280
cactgcgcct gcggggeggc ctttgtggac ttcctgctgg agagacagga ggccgtgccc 2340
gggctgtcca ggcgcgtcac atgtggcagt ccgggccagc tccagggccg cagcatcttc 2400
acacaggacc tgcgcctctg cctggatgag accctctcct tggactgctt tggc 2454

<210> 13

<211> 1031

<212> PRT

<213> Equus caballus

<400> 13

Met Gly Pro Cys His Gly Ala Leu Gln Pro Leu Ser Leu Leu Val Gln

1 10 15

Ala Ala Met Leu Ala Val Ala Leu Ala Gln Gly Thr Leu Pro Pro Phe 20 25 30

Leu Pro Cys Glu Leu Gln Pro His Gly Leu Val Asn Cys Asn Trp Leu 35 40 . 45

Phe Leu Lys Ser Val Pro His Phe Ser Ala Ala Pro Arg Asp Asn 50 55

Val Thr Ser Leu Ser Leu Ser Asn Arg Ile His His Leu His Asp 65 70 75 80

Ser Asp Phe Ala Gln Leu Ser Asn Leu Gln Lys Leu Asn Leu Lys Trp 85 90 95

Asn Cys Pro Pro Ala Gly Leu Ser Pro Met His Phe Pro Cys His Met 100 105 110

Thr Ile Glu Pro Asn Thr Phe Leu Ala Val Pro Thr Leu Glu Glu Leu 115 120 125

Asn Leu Ser Tyr Asn Gly Ile Thr Thr Val Pro Ala Leu Pro Ser Ser 130 135 140

Leu Val Ser Leu Ile Leu Ser Arg Thr Asn Ile Leu Gln Leu Asp Pro 145 150 155 160

Thr Ser Leu Thr Gly Leu His Ala Leu Arg Phe Leu Tyr Met Asp Gly 165 170 175

- Asn Cys Tyr Tyr Lys Asn Pro Cys Gly Arg Ala Leu Glu Val Ala Pro 180 185 190
- Gly Ala Leu Leu Gly Leu Gly Asn Leu Thr His Leu Ser Leu Lys Tyr 195 200 205
- Asn Asn Leu Thr Thr Val Pro Arg Ser Leu Pro Pro Ser Leu Glu Tyr 210 215 220
- Leu Leu Ser Tyr Asn His Ile Val Thr Leu Ala Pro Glu Asp Leu 225 230 235 240
- Ala Asn Leu Thr Ala Leu Arg Val Leu Asp Val Gly Gly Asn Cys Arg 245 250 255
- Arg Cys Asp His Ala Arg Asn Pro Cys Val Glu Cys Pro His Lys Phe 260 265 270
- Pro Gln Leu His Ser Asp Thr Phe Ser His Leu Ser Arg Leu Glu Gly 275 280 285
- Leu Val Leu Lys Asp Ser Ser Leu Tyr Gln Leu Asn Pro Arg Trp Phe 290 295 300
- Arg Gly Leu Gly Asn Leu Thr Val Leu Asp Leu Ser Glu Asn Phe Leu 305 310 315 320
- Tyr Asp Cys Ile Thr Lys Thr Lys Ala Phe Gln Gly Leu Ala Gln Leu 325 330 335
- Arg Arg Leu Asn Leu Ser Phe Asn Tyr His Lys Lys Val Ser Phe Ala 340 345 350
- His Leu Thr Leu Ala Pro Ser Phe Gly Ser Leu Leu Ser Leu Gln Glu 355 360 365
- Leu Asp Met His Gly Ile Phe Phe Arg Ser Leu Ser Gln Lys Thr Leu 370 375 380
- Gln Pro Leu Ala Arg Leu Pro Met Leu Gln Arg Leu Tyr Leu Gln Met 385 390 395 400

١,

Asn Phe Ile Asn Gln Ala Gln Leu Gly Ile Phe Lys Asp Phe Pro Gly 405 410 415

Leu Arg Tyr Ile Asp Leu Ser Asp Asn Arg Ile Ser Gly Ala Val Glu 420 425 430

Pro Val Ala Thr Thr Gly Glu Val Asp Gly Gly Lys Lys Val Trp Leu 435 440 445

Thr Ser Arg Asp Leu Thr Pro Gly Pro Leu Asp Thr Pro Ser Ser Glu 450 455 460

Asp Phe Met Pro Ser Cys Lys Asn Leu Ser Phe Thr Leu Asp Leu Ser 465 470 475 480

Arg Asn Asn Leu Val Thr Val Gln Pro Glu Met Phe Ala Gln Leu Ser 485 490 495

Arg Leu Gln Cys Leu Arg Leu Ser His Asn Ser Ile Ser Gln Ala Val 500 505 510

Asn Gly Ser Gln Phe Val Pro Leu Thr Ser Leu Gln Val Leu Asp Leu 515 520 525

Ser His Asn Lys Leu Asp Leu Tyr His Gly Arg Ser Phe Thr Glu Leu 530 535 540

Pro Arg Leu Glu Ala Leu Asp Leu Ser Tyr Asn Ser Gln Pro Phe Ser 545 550 555 555

Met Arg Gly Val Gly His Asn Leu Ser Phe Val Ala Gln Leu Pro Thr 565 570 575

Leu Arg Tyr Leu Ser Leu Ala His Asn Gly Ile His Ser Arg Val Ser 580 585 590

Gln Gln Leu Cys Ser Thr Ser Leu Trp Ala Leu Asp Phe Ser Gly Asn 595 600 605

Ser Leu Ser Gln Met Trp Ala Glu Gly Asp Leu Tyr Leu Arg Phe Phe 610 615 620

Gln Gly Leu Arg Ser Leu Ile Arg Leu Asp Leu Ser Gln Asn Arg Leu 625 630 635 640

His Thr Leu Leu Pro Cys Thr Leu Gly Asn Leu Pro Lys Ser Leu Gln 645 655

- Leu Leu Arg Leu Arg Asn Asn Tyr Leu Ala Phe Phe Asn Trp Ser Ser 660 665 670
- Leu Thr Leu Leu Pro Asn Leu Glu Thr Leu Asp Leu Ala Gly Asn Gln 675 680 685
- Leu Lys Ala Leu Ser Asn Gly Ser Leu Pro Ser Gly Thr Gln Leu Gln 690 695 700
- Arg Leu Asp Val Ser Arg Asn Ser Ile Ile Phe Val Val Pro Gly Phe 705 710 715 720
- Phe Ala Leu Ala Thr Arg Leu Arg Glu Leu Asn Leu Ser Ala Asn Ala 725 730 735
- Leu Arg Thr Glu Glu Pro Ser Trp Phe Gly Phe Leu Ala Gly Ser Leu 740 745 750
- Glu Val Leu Asp Val Ser Ala Asn Pro Leu His Cys Ala Cys Gly Ala 755 760 765
- Ala Phe Val Asp Phe Leu Leu Gln Val Gln Ala Ala Val Pro Gly Leu 770 780
- Pro Ser Arg Val Lys Cys Gly Ser Pro Gly Gln Leu Gln Gly Arg Ser 785 790 795 800
- Ile Phe Ala Gln Asp Leu Arg Leu Cys Leu Asp Lys Ser Leu Ser Trp 805 810 815
- Asp Cys Phe Gly Leu Ser Leu Leu Val Val Ala Leu Gly Leu Ala Met 820 825 830
- Pro Met Leu His His Leu Cys Gly Trp Asp Leu Trp Tyr Cys Phe His 835
- Leu Gly Leu Ala Trp Leu Pro Arg Arg Gly Trp Gln Arg Gly Ala Asp 850 860
- Ala Leu Ser Tyr Asp Ala Phe Val Val Phe Asp Lys Ala Gln Ser Ala

865 870 875 880

Val Ala Asp Trp Val Tyr Asn Glu Leu Arg Val Arg Leu Glu Glu Arg 885 890 895

Arg Gly Arg Arg Ala Leu Arg Leu Cys Leu Glu Glu Arg Asp Trp Leu 900 905 910

Pro Gly Lys Thr Leu Phe Glu Asn Leu Trp Ala Ser Val Tyr Ser Ser 915 920 925

Arg Lys Met Leu Phe Val Leu Ala His Thr Asp Gln Val Ser Gly Leu 930 935 940

Leu Arg Ala Ser Phe Leu Leu Ala Gln Gln Arg Leu Leu Glu Asp Arg 945 950 955 960

Lys Asp Val Val Leu Val Ile Leu Ser Pro Asp Ala Arg Arg Ser 965 970 975

Arg Tyr Val Arg Leu Arg Gln Arg Leu Cys Arg Gln Ser Val Leu Phe 980 985 990

Trp Pro His Gln Pro Ser Gly Gln Arg Ser Phe Trp Ala Gln Leu Gly 995 1000 1005

Met Ala Leu Thr Arg Asp Asn Arg His Phe Tyr Asn Gln Asn Phe 1010 1015 1020

Cys Arg Gly Pro Thr Met Ala Glu 1025 1030

<210> 14

<211> 820

<212> PRT

<213> Equus caballus

<400> 14

Met Gly Pro Cys His Gly Ala Leu Gln Pro Leu Ser Leu Leu Val Gln
1 5 10 15

Ala Ala Met Leu Ala Val Ala Leu Ala Gln Gly Thr Leu Pro Pro Phe 20 25 30

Leu Pro Cys Glu Leu Gln Pro His Gly Leu Val Asn Cys Asn Trp Leu

35 40 45

Phe Leu Lys Ser Val Pro His Phe Ser Ala Ala Ala Pro Arg Asp Asn 50 55 60

Val Thr Ser Leu Ser Leu Leu Ser Asn Arg Ile His His Leu His Asp 65 70 75 80

Ser Asp Phe Ala Gln Leu Ser Asn Leu Gln Lys Leu Asn Leu Lys Trp 85 90 95

Asn Cys Pro Pro Ala Gly Leu Ser Pro Met His Phe Pro Cys His Met 100 105 110

Thr Ile Glu Pro Asn Thr Phe Leu Ala Val Pro Thr Leu Glu Glu Leu 115 120 125

Asn Leu Ser Tyr Asn Gly Ile Thr Thr Val Pro Ala Leu Pro Ser Ser 130 135 140

Leu Val Ser Leu Ile Leu Ser Arg Thr Asn Ile Leu Gln Leu Asp Pro 145 150 155 160

Thr Ser Leu Thr Gly Leu His Ala Leu Arg Phe Leu Tyr Met Asp Gly 165 170 175

Asn Cys Tyr Tyr Lys Asn Pro Cys Gly Arg Ala Leu Glu Val Ala Pro 180 185 190

Gly Ala Leu Leu Gly Leu Gly Asn Leu Thr His Leu Ser Leu Lys Tyr 195 200 205

Asn Asn Leu Thr Thr Val Pro Arg Ser Leu Pro Pro Ser Leu Glu Tyr 210 215 220

Leu Leu Ser Tyr Asn His Ile Val Thr Leu Ala Pro Glu Asp Leu 225 230 235 235 240

Ala Asn Leu Thr Ala Leu Arg Val Leu Asp Val Gly Gly Asn Cys Arg 245 250 255

Arg Cys Asp His Ala Arg Asn Pro Cys Val Glu Cys Pro His Lys Phe 260 265 270

- 41 -

Pro Gln Leu His Ser Asp Thr Phe Ser His Leu Ser Arg Leu Glu Gly 275 280 285

- Leu Val Leu Lys Asp Ser Ser Leu Tyr Gln Leu Asn Pro Arg Trp Phe 290 295 300
- Arg Gly Leu Gly Asn Leu Thr Val Leu Asp Leu Ser Glu Asn Phe Leu 305 310 315 320
- Tyr Asp Cys Ile Thr Lys Thr Lys Ala Phe Gln Gly Leu Ala Gln Leu 325 330 335
- Arg Arg Leu Asn Leu Ser Phe Asn Tyr His Lys Lys Val Ser Phe Ala 340 345 350
- His Leu Thr Leu Ala Pro Ser Phe Gly Ser Leu Leu Ser Leu Gln Glu 355 360 365
- Leu Asp Met His Gly Ile Phe Phe Arg Ser Leu Ser Gln Lys Thr Leu 370 375 380
- Gln Pro Leu Ala Arg Leu Pro Met Leu Gln Arg Leu Tyr Leu Gln Met 385 390 395 400
- Asn Phe Ile Asn Gln Ala Gln Leu Gly Ile Phe Lys Asp Phe Pro Gly 405 410 415
- Leu Arg Tyr Ile Asp Leu Ser Asp Asn Arg Ile Ser Gly Ala Val Glu
 420 425 430
- Pro Val Ala Thr Thr Gly Glu Val Asp Gly Gly Lys Lys Val Trp Leu 435 440 445
- Thr Ser Arg Asp Leu Thr Pro Gly Pro Leu Asp Thr Pro Ser Ser Glu 450 455 460
- Asp Phe Met Pro Ser Cys Lys Asn Leu Ser Phe Thr Leu Asp Leu Ser 465 470 475 480
- Arg Asn Asn Leu Val Thr Val Gln Pro Glu Met Phe Ala Gln Leu Ser 485 490 495
- Arg Leu Gln Cys Leu Arg Leu Ser His Asn Ser Ile Ser Gln Ala Val 500 505 510

Asn Gly Ser Gln Phe Val Pro Leu Thr Ser Leu Gln Val Leu Asp Leu 515 520 525

- Ser His Asn Lys Leu Asp Leu Tyr His Gly Arg Ser Phe Thr Glu Leu 530 535 540
- Pro Arg Leu Glu Ala Leu Asp Leu Ser Tyr Asn Ser Gln Pro Phe Ser 545 550 555 560
- Met Arg Gly Val Gly His Asn Leu Ser Phe Val Ala Gln Leu Pro Thr 565 570 575
- Leu Arg Tyr Leu Ser Leu Ala His Asn Gly Ile His Ser Arg Val Ser 580 585 590
- Gln Gln Leu Cys Ser Thr Ser Leu Trp Ala Leu Asp Phe Ser Gly Asn 595 600 605
- Ser Leu Ser Gln Met Trp Ala Glu Gly Asp Leu Tyr Leu Arg Phe Phe 610 620
- Gln Gly Leu Arg Ser Leu Ile Arg Leu Asp Leu Ser Gln Asn Arg Leu 625 630 635 640
- His Thr Leu Leu Pro Cys Thr Leu Gly Asn Leu Pro Lys Ser Leu Gln 645 650 655
- Leu Leu Arg Leu Arg Asn Asn Tyr Leu Ala Phe Phe Asn Trp Ser Ser 660 665 670
- Leu Thr Leu Leu Pro Asn Leu Glu Thr Leu Asp Leu Ala Gly Asn Gln 675 680 685
- Leu Lys Ala Leu Ser Asn Gly Ser Leu Pro Ser Gly Thr Gln Leu Gln 690 695 700
- Arg Leu Asp Val Ser Arg Asn Ser Ile Ile Phe Val Val Pro Gly Phe 705 710 715 720
- Phe Ala Leu Ala Thr Arg Leu Arg Glu Leu Asn Leu Ser Ala Asn Ala 725 730 735
- Leu Arg Thr Glu Glu Pro Ser Trp Phe Gly Phe Leu Ala Gly Ser Leu 740 745 750

ده سيست

Glu Val Leu Asp Val Ser Ala Asn Pro Leu His Cys Ala Cys Gly Ala 755 760 765

Ala Phe Val Asp Phe Leu Leu Gln Val Gln Ala Ala Val Pro Gly Leu 770 780

Pro Ser Arg Val Lys Cys Gly Ser Pro Gly Gln Leu Gln Gly Arg Ser 785 790 795 800

Ile Phe Ala Gln Asp Leu Arg Leu Cys Leu Asp Lys Ser Leu Ser Trp 805 810 815

Asp Cys Phe Gly 820

<210> 15 <211> 3391 <212> DNA

<213> Equus caballus

<400> 15

ctctgttctc tgagctgttg ccgcgtgaag ggactgcgag cacaaagcat cctcctctgc 60 agetgetgee cagtgtgeea getggaceet etggateate teccaeteee tgteatggge 120 cettgccatg gtgccctgca gcccctgtct ctcctggtgc aggcggccat gctggccgtg 180 getetggece aaggeaceet geétecette etgecetgtg agetecagee ceaeggeetg 240 gtgaactgca actggctgtt cctgaagtcc gtgccccact tctcagcagc agcaccccgg 300 gacaatgtca ccagcettte ettgetetee aaccqcatce accaceteca eqactecqae 360 tttgcccaac tgtccaacct gcagaaactc aacctcaaat ggaactgccc gccagccggc 420 ctcagcccca tgcacttccc ctgccacatg accatcgagc ccaacacttt cctggctgta 480 cccaccetgg aggagetgaa cctgagetac aacggcatca cgactgtgcc tgccctgccc 540 ageteceteg tgtecetgat cetgageege accaacatee tgcagetaga ecceaceage 600 ctcacgggcc tgcatgccct gcgcttccta tacatggatg gcaactgcta ctacaagaac 660 ccctgcgggc gggccctgga ggtggcccca ggcgccctcc ttggcctggg caacctcacc 720 cacctgtcac tcaagtacaa caacctcaca aoggtgccc gcagcctgcc ccctagcctg. 780 gagtacctgc tgttgtccta caaccacatt gtcaccctgg cacctgagga cctggccaat 840 etgactgccc tgcgtgtgct cgatgtgggt ggaaactgcc gccgctgtga ccatgcacgc 900 960 aacccctgcg tggagtgccc acataaattc ccccagctgc actccgacac cttcagccac

ctaagccgcc	tagaaggcct	cgtgttgaag	gatagttctc	tctaccagct	gaaccccaga	1020
tggttccgtg	gcctgggcaa	cctcacagtg	ctcgacctga	gtgagaactt	cctctacgac	1080
tgcatcacca	aaaccaaggc	attccagggc	ctggcccagc	tgcgaagact	caacttgtcc	1140
ttcaattacc	ataagaaggt	gtccttcgcc	cacetgaege	tggcaccctc	cttcgggagc	1200
ctgctctccc	tgcaggaact	ggacatgcat	ggcatcttct	teegeteact	cagccagaag	1260
acgctccagc	cactggcccg	cctgcccatg	ctccagcgtc	tgtatctgca	gatgaacttc	1320
atcaaccagg	cccagctcgg	catcttcaag	gacttccctg	gtctgcgcta	catagacctg	1380
tcagacaacc	gcatcagtgg	agctgtggag	ccggtggcca	ccacagggga	ggtggatggt	1440
gggaagaagg	tctggctgac	atccagggac	ctcactccag	gcccactgga	caccccagc	1500
tctgaggact	tcatgccaag	ctgcaagaac	ctcagcttca	ccttggacct	gtcacggaac	1560
aacctggtaa	cagtccagcc	agagatgttt	gcccagctct	cgcgcctcca	gtgcctgcgc	1620
ctgagccaca	acagcatete	gcaggcggtc	aatggctcac	agttcgtgcc	actgaccagc	1680
ctgcaggtgc	tggacctgtc	ccataacaaa	ctggacctgt	accatgggcg	ctcgtttacg	1740
gagctgccgc	gaetggagge	cctggacctc	agctacaaca	gccagccctt	cagcatgcgg	1800
ggtgtgggcc	acaacctcag	ctttgtggcc	cagetgeeca	ccctgcgcta	cctcagcctg	1860
gcacacaatg	gcatccacag	ccgtgtgtcc	cagcagctct	gcagcacctc	gctgtgggcc	1920
ctggacttca	gcggcaattc	cctgagccag	atgtgggctg	agggagacct	ctatctccgc	1980
ttcttccaag	gcctgagaag	cctaatccgg	ctagacctgt	cccagaatcg	tctgcatacc	2040
ctcctgccat	gcaccctggg	caacctcccc	aagagettge	agctgctgcg	tctccgtaac	2100
aattacctgg	ccttcttcaa	ttggagcagc	ctgaccctcc	tgcccaacct	ggaaaccctg	2160
gacctggctg	gaaaccagct	gaaggctctg	agcaatggca	gcctgccttc	tggcacccag	2220
ctccagaggc	tggacgtcag	caggaacagc	atcatcttcg	tggtccctgg	cttctttgct	2280
ctggccacga	ggctgcgaga	gctcaacctc	agtgccaacg	ccctcaggac	agaggagccc	2340
tcctggtttg	gtttcctagc	aggctccctt	gaagtcctag	atgtgagcgc	caaccctctg	2400
cactgcgcct	gtggggcagc	ctttgtggac	ttcctgctgc	aggttcaggc	tgccgtgcct	2460
ggtctgccca	gccgcgtcaa	gtgtggcagt	ccgggccagc	tccagggccg	cagcatcttc.	2520 :-
gcacaagacc	tgcgcctctg	cctggacaag	teceteteet	gggactgttt	tggtctctca	2580
ttgctggttg	tggccctggg	cctggccatg	cctatgttgc	accacctctg	c ggctgggac	2640
ctctggtact	gcttccacct	gggcctggcc	tggctgcccc	ggcgggggtg	gcagcggggc	2700

gcggatgccc	tgagctatga	tgcctttgtg	gtcttcgaca	aggcacagag	cgcagtggcc	2760
gactgggtgt	acaatgaact	gcgggtgcgg	ctagaggagc	gccgtgggcg	ccgggcgctc	2820
cgcctgtgtc	tggaggagcg	tgactggcta	cctggcaaga	cgctgttcga	aaacctgtgg	2880
gcctcagtct	acagcagccg	caagatgctg	tttgtgctgg	cccacacgga	ccaggtcagt	2940
ggcctcttgc	gtgccagctt	cctgctggcc	cagcagcgtc	tgctggagga	ccgcaaggac	3000
gttgtggtgc	tggtaatcct	gagecetgae	gcccgccgtt	cccgttacgt	gcggctgcgc	3060
cagcgcctct	gccgccagag	tgtcctcttc	tggccccacc	agcctagtgg	ccagcgcagc	3120
ttctgggccc	agctaggcat	ggccctgacc	agggacaacc	gccacttcta	taaccagaac	3180
ttctgccggg	gcccgacgat	ggctgagtag	cacagagtga	cagcctggca	tgtacaaccc	3240
ccagccctga	ccttgcctct	ctgcctatga	tgcccagtct	gcctcactct	gtgacgcccc	3300
tgctctgcct	ccgccaccct	cacccctggc	atacagcagg	cactcaataa	atgccactgg	3360
caggccaaac	agccaaaaaa	aaaaaaaaa	a	·		3391

<210> 16

<211> 2460

<212> DNA

<213> Equus caballus

atgggccctt gccatggtgc cctgcagccc ctgtctctcc tggtgcaggc ggccatgctg 60 geogtggete tggeccaagg caccetgeet ceetteetge cetgtgaget ceagecceae 120 ggcctggtga actgcaactg gctgttcctg aagtccgtgc cccacttctc agcagcagca 180 ccccgggaca atgtcaccag cettteettg etetecaacc geatecaeca cetecaegae 240 tecgaetttg eccaaetgte caacetgeag aaactcaace teaaatggaa etgeeegeea 300 gccggcctca gccccatgca cttcccctgc cacatgacca tcgagcccaa cactttcctg 360 gctgtaccca ccctggagga gctgaacctg agctacaacg gcatcacgac tgtgcctgcc 420 480 ctgcccagct ccctcgtgtc cctgatcctg agccgcacca acatcctgca gctagacccc accagoetea egggeetgea tgeeetgege tteetataca tggatggeaa etgetaetae 540 aagaacccct gcgggcgggc cctggaggtg gccccaggcg ccctccttgg cctgggcaac 600 ctcacccace tgtcactcaa gtacaacaac ctcacaacgg tgccccgcag cctgcccct 660 agectggagt acctgetgtt gtectacaac cacattgtea ceetggeace tgaggacetg 720 gccaatctga ctgcctgcg tgtgctcgat gtgggtggaa actgccgccg ctgtgaccat 780 gcacgcaacc cctgcgtgga gtgcccacat aaattccccc agctgcactc cgacaccttc 840

· ...

agccacctaa	gccgcctaga	aggcctcgtg	ttgaaggata	gttctctcta	ccagctgaac	900
cccagatggt	tccgtggcct	gggcaacctc	acagtgctcg	acctgagtga	gaacttcctc	960
tacgactgca	tcaccaaaac	caaggcattc	cagggcctgg	cccagctgcg	aagactcaac	1020
ttgtccttca	attaccataa	gaaggtgtcc	ttcgcccacc	tgacgctggc	accctccttc	1080
gggagcctgc	tctccctgca	ggaactggac	atgcatggca	tcttcttccg	ctcactcagc	1140
cagaagacgc	tccagccact	ggcccgcctg	cccatgctcc	agcgtctgta	tctgcagatg	1200
aacttcatca	accaggccca	gctcggcatc	ttcaaggact	tccctggtct	gcgctacata	1260
gacctgtcag	acaaccgcat	cagtggagct	gtggagccgg	tggccaccac	aggggaggtg	1320
gatggtggga	agaaggtctg	gctgacatcc	agggacctca	ctccaggccc	actggacacc	1380
cccagctctg	aggacttcat	gccaagctgc	aagaacctca	gcttcacctt	ggacctgtca	1440
cggaacaacc	tggtaacagt	ccagccagag	atgtttgccc	agctctcgcg	cctccagtgc	1500
ctgcgcctga	gccacaacag	catctcgcag	gcggtcaatg	gctcacagtt	cgtgccactg	1560
accagcetge	aggtgctgga	cctgtcccat	aacaaactgg	acctgtacca	tgggcgctcg	1620
tttacggagc	tgccgcgact	ggaggccctg	gacctcagct	acaacagcca	gcccttcagc	1680
atgcggggtg	tgggccacaa	cctcagcttt	gtggcccagc	tgcccaccct	gcgctacctc	1740
agcctggcac	acaatggcat	ccacagccgt	gtgtcccagc	agctctgcag	cacctcgctg	1800
tgggccctgg	acttcagcgg	caattccctg	agccagatgt	gggctgaggg	agacctctat	1860
ctccgcttct	tccaaggcct	gagaagccta	atccggctag	acctgtccca	gaatcgtctg	1920
cataccctcc	tgccatgcac	cctgggcaac	ctccccaaga	gcttgcagct	getgegtete	1980
cgtaacaatt	acctggcctt	cttcaattgg	agcagcctga	ccctcctgcc	caacctggaa	2040
accctggacc	tggctggaaa	ccagctgaag	gctctgagca	atggcagcct	gccttctggc	2100
acccagetee	agaggctgga	cgtcagcagg	aacagcatca	tcttcgtggt	ccctggcttc	2160
tttgctctgg	ccacgagget	gcgagagctc	aacctcagtg	ccaacgccct	caggacagag	2220
gagccctcct	ggtttggttt	cctagcaggc	tcccttgaag	tcctagatgt	gagcgccaac	2280
cctctgcact	gcgcctgtgg	ggcagccttt	gtggacttcc	tgctgcaggt	tcaggctgcc	2340
gtgcctggtc	tgcccagccg	cgtcaagtgt	ggcagtccgg	gccagctcca	gggccgcagc	2400
atettegeae	aagacctgcg	cctctgcctg	gacaagtccc	tctcctggga	ctgttttggt	2460

<210> 17 <211> 1029 <212> PRT

<213> Ovis aries

<400> 17

Met Gly Pro Tyr Cys Ala Pro His Pro Leu Ser Leu Leu Val Gln Ala 1 5 10 15

Ala Ala Leu Ala Ala Leu Ala Gln Gly Thr Leu Pro Ala Phe Leu 20 25 30

Pro Cys Glu Leu Gln Pro Arg Gly Lys Val Asn Cys Asn Trp Leu Phe 35 40 45

Leu Lys Ser Val Pro Arg Phe Ser Ala Gly Ala Pro Arg Ala Asn Val 50 55 60

Thr Ser Leu Ser Leu Ile Ser Asn Arg Ile His His Leu His Asp Ser 65 70 75 80

Asp Phe Val His Leu Ser Asn Leu Arg Val Leu Asn Leu Lys Trp Asn 85 90 95

Cys Pro Pro Ala Gly Leu Ser Pro Met His Phe Pro Cys Arg Met Thr 100 105 110

Ile Glu Pro Asn Thr Phe Leu Ala Val Pro Thr Leu Glu Glu Leu Asn 115 120 125

Leu Ser Tyr Asn Gly Ile Thr Thr Val Pro Ala Leu Pro Ser Ser Leu 130 135 140

Val Ser Leu Ser Leu Ser Arg Thr Ser Ile Leu Val Leu Gly Pro Thr 145 150 155 160

His Phe Thr Gly Leu His Ala Leu Arg Phe Leu Tyr Met Asp Gly Asn 165 170 175

Cys Tyr Tyr Lys Asn Pro Cys Gln Gln Ala Val Glu Val Ala Pro Gly 180 185 190

Ala Leu Leu Gly Leu Gly Asn Leu Thr His Leu Ser Leu Lys Tyr Asn 195 200 205 205

Asn Leu Thr Glu Val Pro Arg Arg Leu Pro Pro Ser Leu Asp Thr Leu 210 215 220

Leu Leu Ser Tyr Asn His Ile Ile Thr Leu Ala Pro Glu Asp Leu Ala 225 235 240

- Asn Leu Thr Ala Leu Arg Val Leu Asp Val Gly Gly Asn Cys Arg Arg 245 250 255
- Cys Asp His Ala Arg Asn Pro Cys Arg Glu Cys Pro Lys Asn Phe Pro 260 265 270
- Lys Leu His Pro Asp Thr Phe Ser His Leu Ser Arg Leu Glu Gly Leu 275 280 285
- Val Leu Lys Asp Ser Ser Leu Tyr Lys Leu Glu Lys Asp Trp Phe Arg 290 295 300
- Gly Leu Gly Arg Leu Gln Val Leu Asp Leu Ser Glu Asn Phe Leu Tyr 305 310 315 320
- Asp Tyr Ile Thr Lys Thr Thr Ile Phe Arg Asn Leu Thr Gln Leu Arg 325 330 335
- Arg Leu Asn Leu Ser Phe Asn Tyr His Lys Lys Val Ser Phe Ala His 340 345 350
- Leu Gln Leu Ala Pro Ser Phe Gly Gly Leu Val Ser Leu Glu Lys Leu 355 360 365
- Asp Met His Gly Ile Phe Phe Arg Ser Leu Thr Asn Thr Thr Leu Arg 370 375 380
- Pro Leu Thr Gln Leu Pro Lys Leu Gln Ser Leu Ser Leu Gln Leu Asn 390 395 400
- Phe Ile Asn Gln Ala Glu Leu Ser Ile Phe Gly Ala Phe Pro Ser Leu 405 410 415
- Leu Phe Val Asp Leu Ser Asp Asn Arg Ile Ser Gly Ala Ala Arg Pro 420 425 430
- Val Ala Ala Leu Gly Glu Val Asp Ser Gly Val Glu Val Trp Arg Trp 435 440 445
- Pro Arg Gly Leu Ala Pro Gly Pro Leu Ala Ala Val Ser Ala Lys Asp 450 455 460

Phe Met Pro Ser Cys Asn Leu Asn Phe Thr Leu Asp Leu Ser Arg Asn 465 . 470 475 480

- Asn Leu Val Thr Ile Gln Gln Glu Met Phe Thr Arg Leu Ser Arg Leu 485 490 495
- Gln Cys Leu Arg Leu Ser His Asn Ser Ile Ser Gln Ala Val Asn Gly 500 505 510
- Ser Gln Phe Val Pro Leu Thr Arg Leu Arg Val Leu Asp Leu Ser Tyr 515 520 525
- Asn Lys Leu Asp Leu Tyr His Gly Arg Ser Phe Thr Glu Leu Pro Gln 530 535 540
- Leu Glu Ala Leu Asp Leu Ser Tyr Asn Ser Gln Pro Phe Ser Met Gln 545 550 555 560
- Gly Val Gly His Asn Leu Ser Phe Val Ala Gln Leu Pro Ser Leu Arg 565 570 575
- Tyr Leu Ser Leu Ala His Asn Gly Ile His Ser Arg Val Ser Gln Lys 580 585 590
- Leu Ser Ser Ala Ser Leu Arg Ala Leu Asp Phe Ser Gly Asn Ser Leu 595 600 605
- Ser Gln Met Trp Ala Glu Gly Asp Leu Tyr Leu Cys Phe Phe Lys Gly 610 615 620
- Leu Arg Asn Leu Val Gln Leu Asp Leu Ser Lys Asn His Leu His Thr 625 630 635 640
- Leu Leu Pro Arg His Leu Asp Asn Leu Pro Lys Ser Leu Arg Gln Leu 645 650 655
- Arg Leu Arg Asp Asn Asn Leu Ala Phe Phe Asn Trp Ser Ser Leu Thr 660 665 670
- Val Leu Pro Gln Leu Glu Ala Leu Asp Leu Ala Gly Asn Gln Leu Lys 675 680 685
- Ala Leu Ser Asn Gly Ser Leu Pro Pro Gly Thr Arg Leu Gln Lys Leu 690 695 700

Asp Val Ser Ser Asn Ser Ile Gly Phe Val Thr Pro Gly Phe Phe Val 705 710 715 720

Leu Ala Asn Arg Leu Lys Glu Leu Asn Leu Ser Ala Asn Ala Leu Lys
725 730 735

Thr Val Asp Pro Phe Trp Phe Gly Arg Leu Thr Glu Thr Leu Asn Ile 740 745 750

Leu Asp Val Ser Ala Asn Pro Leu His Cys Ala Cys Gly Ala Ala Phe
755 760 765

Val Asp Phe Leu Leu Glu Met Gln Ala Ala Val Pro Gly Leu Ser Arg 770 780

Arg Val Thr Cys Gly Ser Pro Gly Gln Leu Gln Gly Arg Ser Ile Phe 785 790 795 800

Ala Gln Asp Leu Arg Leu Cys Leu Asp Glu Thr Leu Ser Leu Asp Cys 805 810 815

Phe Gly Phe Ser Leu Leu Met Val Ala Leu Gly Leu Ala Val Pro Met 820 825 830

Leu His His Leu Cys Gly Trp Asp Leu Trp Tyr Cys Phe His Leu Cys 835 840 845

Leu Ala His Leu Pro Arg Arg Arg Gln Arg Gly Glu Asp Thr Leu 850 855 860

Leu Tyr Asp Ala Phe Val Val Phe Asp Lys Ala Gln Ser Ala Val Ala 865 870 875 880

Asp Trp Val Tyr Asn Glu Leu Arg Val Gln Leu Glu Glu Arg Arg Gly 885 890 895

Arg Arg Ala Leu Arg Leu Cys Leu Glu Glu Arg Asp Trp Leu Pro Gly 900 905 910

Lys Thr Leu Phe Glu Asn Leu Trp Ala Ser Val Tyr Ser Ser Arg Lys 915 920 925

Thr Met Phe Val Leu Asp His Thr Asp Arg Val Ser Gly Leu Leu Arg

930 935 940

Ala Ser Phe Leu Leu Ala Gln Gln Arg Leu Leu Glu Asp Arg Lys Asp 945 950 955 960

Val Val Leu Val Ile Leu Arg Pro Ala Ala Tyr Arg Ser Arg Tyr 965 970 975

Val Arg Leu Arg Gln Arg Leu Cys Arg Gln Ser Val Leu Leu Trp Pro 980 985 990

His Gln Pro Ser Gly Gln Gly Ser Phe Trp Ala Asn Leu Gly Met Ala 995 1000 1005

Leu Thr Arg Asp Asn Arg His Phe Tyr Asn Arg Asn Phe Cys Arg 1010 1015 1020

Gly Pro Thr Thr Ala Glu 1025

<210> 18

<211> 818

<212> PRT

<213> Ovis aries

<400> 18

Met Gly Pro Tyr Cys Ala Pro His Pro Leu Ser Leu Leu Val Gln Ala 1 5 10 15

· Ala Ala Leu Ala Ala Leu Ala Gln Gly Thr Leu Pro Ala Phe Leu 20 25 30

Pro Cys Glu Leu Gln Pro Arg Gly Lys Val Asn Cys Asn Trp Leu Phe 35 40 45

Leu Lys Ser Val Pro Arg Phe Ser Ala Gly Ala Pro Arg Ala Asn Val 50 55 60

Thr Ser Leu Ser Leu Ile Ser Asn Arg Ile His His Leu His Asp Ser 65 70 75 80

Asp Phe Val His Leu Ser Asn Leu Arg Val Leu Asn Leu Lys Trp Asn 85 90 95

Cys Pro Pro Ala Gly Leu Ser Pro Met His Phe Pro Cys Arg Met Thr

100 105 ' 110

Ile Glu Pro Asn Thr Phe Leu Ala Val Pro Thr Leu Glu Glu Leu Asn 115 120 125

Leu Ser Tyr Asn Gly Ile Thr Thr Val Pro Ala Leu Pro Ser Ser Leu 130 140

Val Ser Leu Ser Leu Ser Arg Thr Ser Ile Leu Val Leu Gly Pro Thr 145 150 155 160

His Phe Thr Gly Leu His Ala Leu Arg Phe Leu Tyr Met Asp Gly Asn 165 170 175

Cys Tyr Tyr Lys Asn Pro Cys Gln Gln Ala Val Glu Val Ala Pro Gly
180 185 190

Ala Leu Leu Gly Leu Gly Asn Leu Thr His Leu Ser Leu Lys Tyr Asn 195 200 205

Asn Leu Thr Glu Val Pro Arg Arg Leu Pro Pro Ser Leu Asp Thr Leu 210 215 220

Leu Leu Ser Tyr Asn His Ile Ile Thr Leu Ala Pro Glu Asp Leu Ala 225 230 235 240

Asn Leu Thr Ala Leu Arg Val Leu Asp Val Gly Gly Asn Cys Arg Arg 245 250 255

Cys Asp His Ala Arg Asn Pro Cys Arg Glu Cys Pro Lys Asn Phe Pro 260 265 270

Lys Leu His Pro Asp Thr Phe Ser His Leu Ser Arg Leu Glu Gly Leu 275 280 285

Val Leu Lys Asp Ser Ser Leu Tyr Lys Leu Glu Lys Asp Trp Phe Arg 290 295 300

Gly Leu Gly Arg Leu Gln Val Leu Asp Leu Ser Glu Asn Phe Leu Tyr 305 310 315 320

Asp Tyr Ile Thr Lys Thr Thr Ile Phe Arg Asn Leu Thr Gln Leu Arg 325 330 335

Arg Leu Asn Leu Ser Phe Asn Tyr His Lys Lys Val Ser Phe Ala His 340 345

- Leu Gln Leu Ala Pro Ser Phe Gly Gly Leu Val Ser Leu Glu Lys Leu 355 360 365
- Asp Met His Gly Ile Phe Phe Arg Ser Leu Thr Asn Thr Thr Leu Arg 370 375 380
- Pro Leu Thr Gln Leu Pro Lys Leu Gln Ser Leu Ser Leu Gln Leu Asn 385 390 395 400
- Phe Ile Asn Gln Ala Glu Leu Ser Ile Phe Gly Ala Phe Pro Ser Leu 405 410 415
- Leu Phe Val Asp Leu Ser Asp Asn Arg Ile Ser Gly Ala Ala Arg Pro 420 425 430
- Val Ala Ala Leu Gly Glu Val Asp Ser Gly Val Glu Val Trp Arg Trp
 435 440 445
- Pro Arg Gly Leu Ala Pro Gly Pro Leu Ala Ala Val Ser Ala Lys Asp 450 455 460
- Phe Met Pro Ser Cys Asn Leu Asn Phe Thr Leu Asp Leu Ser Arg Asn 465 470 475 480
- Asn Leu Val Thr Ile Gln Gln Glu Met Phe Thr Arg Leu Ser Arg Leu 485 490 495
- Gln Cys Leu Arg Leu Ser His Asn Ser Ile Ser Gln Ala Val Asn Gly 500 505 510
- Ser Gln Phe Val Pro Leu Thr Arg Leu Arg Val Leu Asp Leu Ser Tyr 515 520 525
- Asn Lys Leu Asp Leu Tyr His Gly Arg Ser Phe Thr Glu Leu Pro Gln 530 535 540
- Leu Glu Ala Leu Asp Leu Ser Tyr Asn Ser Gln Pro Phe Ser Met Gln 545 550 555 560
- Gly Val Gly His Asn Leu Ser Phe Val Ala Gln Leu Pro Ser Leu Arg 565 570 575

Tyr Leu Ser Leu Ala His Asn Gly Ile His Ser Arg Val Ser Gln Lys
580 585 590

- Leu Ser Ser Ala Ser Leu Arg Ala Leu Asp Phe Ser Gly Asn Ser Leu 595 600 605
- Ser Gln Met Trp Ala Glu Gly Asp Leu Tyr Leu Cys Phe Phe Lys Gly 610 620
- Leu Arg Asn Leu Val Gln Leu Asp Leu Ser Lys Asn His Leu His Thr 625 630 635 640
- Leu Leu Pro Arg His Leu Asp Asn Leu Pro Lys Ser Leu Arg Gln Leu 645 650 655
- Arg Leu Arg Asp Asn Asn Leu Ala Phe Phe Asn Trp Ser Ser Leu Thr 660 665 670
- Val Leu Pro Gln Leu Glu Ala Leu Asp Leu Ala Gly Asn Gln Leu Lys 675 680 685
- Ala Leu Ser Asn Gly Ser Leu Pro Pro Gly Thr Arg Leu Gln Lys Leu 690 695 700
- Asp Val Ser Ser Asn Ser Ile Gly Phe Val Thr Pro Gly Phe Phe Val 705 710 715 720
- Leu Ala Asn Arg Leu Lys Glu Leu Asn Leu Ser Ala Asn Ala Leu Lys 725 730 735
- Thr Val Asp Pro Phe Trp Phe Gly Arg Leu Thr Glu Thr Leu Asn Ile 740 745 750
- Leu Asp Val Ser Ala Asn Pro Leu His Cys Ala Cys Gly Ala Ala Phe 755 760 765
- Val Asp Phe Leu Leu Glu Met Gln Ala Ala Val Pro Gly Leu Ser Arg 770 775 780
- Arg Val Thr Cys Gly Ser Pro Gly Gln Leu Gln Gly Arg Ser Ile Phe 785 790 795 800
- Ala Gln Asp Leu Arg Leu Cys Leu Asp Glu Thr Leu Ser Leu Asp Cys 805 810 815

Phe Gly

<210> 19

3199 <212> DNA <213> Ovis aries <400> 19 gtcggcacgg gaagtgagcg ccaagcatcc ttccctgcag ctgccgccca acttgcccgc 60 cagaccetet ggagaageeg cattecetge catgggeece tactgtgeec egeacceet 120 ttctctcctg gtgcaggcgg cggcgctggc agcagccctg gcccagggca ccctgcctgc 180 cttcctgccc tgtgagctcc agccccgggg taaggtgaac tgcaactggc tgttcctgaa 240 gtotgtgccg cgcttttcgg ccggagcccc ccgggccaat gtcaccagcc tctccttaat 300 ctccaaccgc atccaccact tgcacgactc tgacttcgtc cacctgtcca acctgcgggt 360 cctcaacctc aagtggaact gcccgccggc cggcctcagc cccatgcact tcccctgccg 420 catgaccatc gagcccaaca ccttcctggc tgtgcccacc ctggaggagc tgaacctgag 480 ctacaatggc atcacgaccg tgcctgccct gcccagttct ctcgtatccc tgtcgctgag 540 coqcaccaqc atcotggtgc taggecocac coacttoacc ggcctgcacg coetgegett 600 tetgtacatg gaeggeaact getactataa gaaceeetge cageaggeeg tggaggtgge 660 cccaggcgcc ctccttggcc tgggcaacct cacgcacctg tcgctcaagt acaacaacct 720 cacggaggtg ccccgccgcc tgccccccag cctggacacc ctgctgctgt cctacaacca 780 catcatcacc ctggcacccg aggacctggc caatctgact gccctgcgtg tgcttgatgt 840 gggcgggaac tgccgccgct gcgaccacgc ccgcaacccc tgcagggagt gcccaaagaa 900 cttccccaag ctgcaccctg acaccttcag ccacctgagc cgcctcgaag gcctggtgtt 960 gaaggacagt tetetetaca aactagagaa agactggtte egeggeetgg geaggeteea 1020 1080 agtgctcgac ctgagtgaga acttcctcta tgactacatc accaagacca ccatcttcag 1140 gaacctgacc cagctgcgca gactcaacct gtccttcaat taccacaaga aggtgtcctt cgcccacctg caactggcac cctcctttgg gggcctggtg tccctggaga agctggacat 1200 gcacggcatc ttcttccgct ccctcaccaa caccacgctc cggccgctga cccagctgcc 1260 caagetecag agtetgagte tgeagetgaa etteateaae caggeegage teageatett 1320 tggggccttc ccgagcctgc tcttcgtgga cctgtcggac aaccgcatca gcggagctgc 1380 gaggccggtg gccgccctcg gggaggtgga cagcggggtg gaagtctggc ggtggcccag 1440

gggcctcgct	ccaggcccgc	tggccgccgt	cagcgcaaag	gacttcatgc	caagctgcaa	1500
cctcaacttc	accttggacc	tgtcacggaa	caacctggtg	acgatccagc	aggagatgtt	1560
tacccgcctc	tecegeetee	agtgcctgcg	cctgagccac	aacagcatct	cgcaggcggt	1620
taatggctcg	cagttcgtgc	cgctgacccg	cctgcgagtg	ctcgacctgt	cctacaacaa	1680
gctggacctg	taccatgggc	gctcgttcac	ggagctgccg	cagctggagg	cactggacct	1740
cagctacaac	agccagccct	tcagcatgca	gggcgtgggc	cacaacetca	gcttcgtggc	1800
ccagctgccg	tccctgcgct	acctcagcct	tgcgcacaac	ggcatccaca	gccgcgtgtc	1860
acagaagctc	agcagcgcct	cgctgcgcgc	cctggacttc	agcggcaact	ccctgagcca	1920
gatgtgggcc	gagggagacc	tctatctctg	cttcttcaaa	ggcttgagga	acctggtcca	1980
gctggacctg	tccaagaacc	acctgcacac	cctcctgcct	cgtcacctgg	ataacctgcc	2040
caagagcctg	cggcagctgc	gtctccggga	caataacctg	gccttcttca	actggagcag	2100
cctgactgtt	ctgccccagc	tggaagccct	ggatctggcg	ggaaaccagc	tgaaggccct	2160
gagcaacggc	agectgeeae	ctggcacccg	gctccagaag	ctggacgtga	gcagcaacag	2220
categgettt	gtgacccctg	gcttctttgt	ccttgccaac	cggctgaaag	agcttaacct	2280
cagcgccaac	gccctgaaga	cagtggatcc	cttctggttc	ggtcgcttaa	cagagaccct	2340
gaatatccta	gacgtgagcg	ccaacccgct	ccactgtgcc	tgcggggcgg	cctttgtgga	2400
cttcctgctg	gagatgcagg	cggccgtgcc	tgggctgtcc	aggcgcgtca	cgtgtggcag	2460
tccgggccag	ctccagggcc	gcagcatctt	cgcacaggac	ctgcgcctct	gcctggatga	2520
gaccctctcc	ttggactgct	ttggcttctc	gctgctaatg	gtggcgctgg	gcctggcggt	2580
gcccatgctg	caccacctct	gtggctggga	cctgtggtac	tgcttccacc	tgtgtctggc	2640
ccatttgccc	cgacggcggc	ggcagcgggg	cgaggacacc	ctgctctacg	atgccttcgt	2700
ggtcttcgac	aaggcgcaga	gtgcagtggc	cgactgggtg	tacaacgagc	teegegtgea	2760
gctggaggag	cgccgcgggc	gccgggcgct	ccgcctctgc	ctggaggagc	gagactggct	2820
ccctggcaag	acgctcttcg	agaacctgtg	ggcctcggtc	tacagcagcc	gtaagaccat	2880
gttcgtgctg	gaccacacgg	accgggtcag	tggcctcctg	cgcgccagct	tectgetgge	2940
ccagcagcgc	ctgttggagg	accgcaagga	tgtcgtggtg	ctggtgatcc	tgcgccccgc	3000
cgcctaccgg	tcccgctacg	tgcggctgcg	ccagcgcctc	tgccgccaga	gcgtcctcct	3060
ctggccccac	cagcccagtg	gccagggtag	cttctgggcc	aacctgggca	tggccctgac	3120
cagggacaac	cgccacttct	ataaccggaa	cttctgccgg	ggccccacga	cagccgaata	3180

gcacagagtg actgcccag 3199

<210> 20 <211> 2454

<212> DNA

<213> Ovis aries

<400> 20 atgggccct actgtgccc gcacccctt tctctcctgg tgcaggcggc ggcgctggca 60 quagecetgq cocagggeac cetgeetgec treetgeeet gtgageteea geeeeggggt 120 aaggtgaact gcaactgget gtteetgaag tetgtgeege gettttegge eggageeece 180 cgggccaatg tcaccageet etecttaate tecaacegea tecaecaett geacgaetet 240 gacttcgtcc acctgtccaa cctgcgggtc ctcaacctca agtggaactg cccgccggcc 300 ggcctcagcc ccatgcactt cccctgccgc atgaccatcg agcccaacac cttcctggct 360 gtgcccaccc tggaggagct gaacctgagc tacaatggca tcacgaccgt gcctgccctg 420 cccagttete tegtatecet gtegetgage egeaceagea teetggtget aggeeecace 480 cacttcaccg gcctgcacgc cctgcgcttt ctgtacatgg acggcaactg ctactataag 540 600 aacccctgcc agcaggccgt ggaggtggcc ccaggcgccc tccttggcct gggcaacctc acquacctgt cgctcaagta caacaacctc acggaggtgc cccgccgcct gccccccagc 660 ctggacaccc tgctgctgtc ctacaaccac atcatcaccc tggcacccga ggacctggcc 720 aatctgactg ccctgcgtgt gcttgatgtg ggcgggaact gccgccgctg cgaccacgcc 780 cgcaaccct gcaggagtg cccaaagaac ttccccaagc tgcaccctga caccttcagc 840 cacctgagec geetegaagg cetggtgttg aaggacagtt etetetacaa actagagaaa 900 gactggttcc gcggcctggg caggctccaa gtgctcgacc tgagtgagaa cttcctctat 960 gactacatca ccaagaccac catcttcagg aacctgaccc agctgcgcag actcaacctg 1020 tectteaatt accacaagaa ggtgteette geecacetge aactggcace etectttggg 1080 ggcctggtgt ccctggagaa gctggacatg cacggcatct tcttccgctc cctcaccaac 1140 accacgetec ggccgctgac ccagetgecc aagetecaga gtetgagtet geagetgaac 1200 ttcatcaacc aggccgagct cagcatcttt ggggccttcc cgagcctgct cttcgtggac 1260 ctgtcggaca accgcatcag cggagctgcg aggccggtgg ccgccctcgg ggaggtggac 1320 ageggggtgg aagtetggeg gtggeecagg ggeetegete caggeeeget ggeegeegte 1380 agegeaaagg actteatgee aagetgeaac eteaaettea eettggaeet gteaeggaae 1440

1500

aacctggtga cgatccagca ggagatgttt acccgcctct cccgcctcca gtgcctgcgc

ctgagccaca	acagcatctc	gcaggcggtt	aatggctcgc	agttegtgee	gctgacccgc	1560
ctgcgagtgc	tcgacctgtc	ctacaacaag	ctggacctgt	accatgggcg	ctcgttcacg	1620
gagctgccgc	agctggaggc	actggacctc	agctacaaca	gccagccctt	cagcatgcag	1680
ggcgtgggcc	acaacctcag	cttcgtggcc	cagctgccgt	ccctgcgcta	cctcagcctt	1740
gcgcacaacg	gcatccacag	ccgcgtgtca	cagaagctca	gcagcgcctc	gctgcgcgcc	1800
ctggacttca	gcggcaactc	cctgagccag	atgtgggccg	agggagacct	ctatctctgc	1860
ttcttcaaag	gcttgaggaa	cctggtccag	ctggacctgt	ccaagaacca	cctgcacacc	1920
ctcctgcctc	gtcacctgga	taacctgccc	aagagcctgc	ggcagctgcg	tctccgggac	1980
aataacctgg	ccttcttcaa	ctggagcagc	ctgactgttc	tgccccagct	ggaagccctg	2040
gatctggcgg	gaaaccagct	gaaggccctg	agcaacggca	gcctgccacc	tggcacccgg	2100
ctccagaagc	tggacgtgag	cagcaacagc	atcggctttg	tgacccctgg	cttctttgtc	2160
cttgccaacc	ggctgaaaga	gcttaacctc	agcgccaacg	ccctgaagac	agtggatccc	2220
ttctggttcg	gtcgcttaac	agagaccctg	aatatcctag	acgtgagcgc	caacccgctc	2280
cactgtgcct	gcggggcggc	ctttgtggac	ttcctgctgg	agatgcaggc	ggccgtgcct	2340
gggctgtcca	ggcgcgtcac	gtgtggcagt	ccgggccagc	tccagggccg	cagcatcttc	2400
gcacaggacc	tgcgcctctg	cctggatgag	accctctcct	tggactgctt	tggc	2454

<210> 21 <211> 1032 <212> PRT

<213> Canis familiaris

<400> 21

Met Gly Pro Cys Arg Gly Ala Leu His Pro Leu Ser Leu Leu Val Gln

Ala Ala Leu Ala Leu Ala Leu Ala Gln Gly Thr Leu Pro Ala Phe

Leu Pro Cys Glu Leu Gln Pro His Gly Leu Val Asn Cys Asn Trp Leu

Phe Leu Lys Ser Val Pro Arg Phe Ser Ala Ala Pro Arg Gly Asn 50

Val Thr Ser Leu Ser Leu Tyr Ser Asn Arg Ile His His Leu His Asp 65 70

Tyr Asp Phe Val His Phe Val His Leu Arg Arg Leu Asn Leu Lys Trp 85 90 95

- Asn Cys Pro Pro Ala Ser Leu Ser Pro Met His Phe Pro Cys His Met
 100 105 110
- Thr Ile Glu Pro Asn Thr Phe Leu Ala Val Pro Thr Leu Glu Asp Leu 115 120 125
- Asn Leu Ser Tyr Asn Ser Ile Thr Thr Val Pro Ala Leu Pro Ser Ser 130 140
- Leu Val Ser Leu Ser Leu Ser Arg Thr Asn Ile Leu Val Leu Asp Pro 145 150 155 160
- Ala Thr Leu Ala Gly Leu Tyr Ala Leu Arg Phe Leu Phe Leu Asp Gly
 165 170 175
- Asn Cys Tyr Tyr Lys Asn Pro Cys Gln Gln Ala Leu Gln Val Ala Pro 180 185 190
- Gly Ala Leu Leu Gly Leu Gly Asn Leu Thr His Leu Ser Leu Lys Tyr 195 200 205
- Asn Asn Leu Thr Val Val Pro Arg Gly Leu Pro Pro Ser Leu Glu Tyr 210 215 220
- Leu Leu Ser Tyr Asn His Ile Ile Thr Leu Ala Pro Glu Asp Leu 225 230 235 240
- Ala Asn Leu Thr Ala Leu Arg Val Leu Asp Val Gly Gly Asn Cys Arg 245 250 255
- Arg Cys Asp His Ala Arg Asn Pro Cys Arg Glu Cys Pro Lys Gly Phe 260 265 270
- Pro Gln Leu His Pro Asn Thr Phe Gly His Leu Ser His Leu Glu Gly 275 280 285
- Leu Val Leu Arg Asp Ser Ser Leu Tyr Ser Leu Asp Pro Arg Trp Phe 290 295 300
- His Gly Leu Gly Asn Leu Met Val Leu Asp Leu Ser Glu Asn Phe Leu 305 310 315 320

Tyr Asp Cys Ile Thr Lys Thr Lys Ala Phe Tyr Gly Leu Ala Arg Leu 325 330 335

- Arg Arg Leu Asn Leu Ser Phe Asn Tyr His Lys Lys Val Ser Phe Ala 340 345
- His Leu His Leu Ala Ser Ser Phe Gly Ser Leu Leu Ser Leu Gln Glu 355 360 365
- Leu Asp Ile His Gly Ile Phe Phe Arg Ser Leu Ser Lys Thr Thr Leu 370 375 380
- Gln Ser Leu Ala His Leu Pro Met Leu Gln Arg Leu His Leu Gln Leu 385 390 395 400
- Asn Phe Ile Ser Gln Ala Gln Leu Ser Ile Phe Gly Ala Phe Pro Gly
 405 410 415
- Leu Arg Tyr Val Asp Leu Ser Asp Asn Arg Ile Ser Gly Ala Ala Glu 420 425 430
- Pro Ala Ala Ala Thr Gly Glu Val Glu Ala Asp Cys Gly Glu Arg Val 435 440 445
- Trp Pro Gln Ser Arg Asp Leu Ala Leu Gly Pro Leu Gly Thr Pro Gly 450 455 460
- Ser Glu Ala Phe Met Pro Ser Cys Arg Thr Leu Asn Phe Thr Leu Asp 465 470 475 480
- Leu Ser Arg Asn Asn Leu Val Thr Val Gln Pro Glu Met Phe Val Arg 485 490 495
- Leu Ala Arg Leu Gln Cys Leu Gly Leu Ser His Asn Ser Ile Ser Gln 500 505 510
- Ala Val Asn Gly Ser Gln Phe Val Pro Leu Ser Asn Leu Arg Val Leu 515 520 525
- Asp Leu Ser His Asn Lys Leu Asp Leu Tyr His Gly Arg Ser Phe Thr 530 540
- Glu Leu Pro Arg Leu Glu Ala Leu Asp Leu Ser Tyr Asn Ser Gln Pro

545 550 555 560

Phe Ser Met Arg Gly Val Gly His Asn Leu Ser Phe Val Ala Gln Leu 565 570 575

Pro Ala Leu Arg Tyr Leu Ser Leu Ala His Asn Gly Ile His Ser Arg 580 585 590

Val Ser Gln Gln Leu Arg Ser Ala Ser Leu Arg Ala Leu Asp Phe Ser 595 600 605

Gly Asn Thr Leu Ser Gln Met Trp Ala Glu Gly Asp Leu Tyr Leu Arg 610 615 620

Phe Phe Gln Gly Leu Arg Ser Leu Val Gln Leu Asp Leu Ser Gln Asn 625 630 635 640

Arg Leu His Thr Leu Leu Pro Arg Asn Leu Asp Asn Leu Pro Lys Ser 645 650 655

Leu Arg Leu Leu Arg Leu Arg Asp Asn Tyr Leu Ala Phe Phe Asn Trp 660 665 670

Ser Ser Leu Ala Leu Leu Pro Lys Leu Glu Ala Leu Asp Leu Ala Gly 675 680 685

Asn Gln Leu Lys Ala Leu Ser Asn Gly Ser Leu Pro Asn Gly Thr Gln 690 695 700

Leu Gln Arg Leu Asp Leu Ser Gly Asn Ser Ile Gly Phe Val Val Pro 705 710 715 720

Ser Phe Phe Ala Leu Ala Val Arg Leu Arg Glu Leu Asn Leu Ser Ala 725 730 735

Asn Ala Leu Lys Thr Val Glu Pro Ser Trp Phe Gly Ser Leu Ala Gly 740 745 750

Ala Leu Lys Val Leu Asp Val Thr Ala Asn Pro Leu His Cys Ala Cys 755 760 765

Gly Ala Thr Phe Val Asp Phe Leu Leu Glu Val Gln Ala Ala Val Pro 770 780

Gly Leu Pro Ser Arg Val Lys Cys Gly Ser Pro Gly Gln Leu Gln Gly 785 790 795 800

- Arg Ser Ile Phe Ala Gln Asp Leu Arg Leu Cys Leu Asp Glu Ala Leu 805 810 815
- Ser Trp Val Cys Phe Ser Leu Ser Leu Leu Ala Val Ala Leu Ser Leu 820 825 830
- Ala Val Pro Met Leu His Gln Leu Cys Gly Trp Asp Leu Trp Tyr Cys 835 840 845
- Phe His Leu Cys Leu Ala Trp Leu Pro Arg Arg Gly Arg Arg Gly 850 855 860
- Val Asp Ala Leu Ala Tyr Asp Ala Phe Val Val Phe Asp Lys Ala Gln 865 870 875 880
- Ser Ser Val Ala Asp Trp Val Tyr Asn Glu Leu Arg Val Gln Leu Glu 885 890 895
- Glu Arg Arg Gly Arg Arg Ala Leu Arg Leu Cys Leu Glu Glu Arg Asp 900 905 910
- Trp Val Pro Gly Lys Thr Leu Phe Glu Asn Leu Trp Ala Ser Val Tyr 915 920 925
- Ser Ser Arg Lys Thr Leu Phe Val Leu Ala Arg Thr Asp Arg Val Ser 930 935 940
- Gly Leu Leu Arg Ala Ser Phe Leu Leu Ala Gln Gln Arg Leu Leu Glu 945 950 955 960
- Asp Arg Lys Asp Val Val Val Leu Val Ile Leu Cys Pro Asp Ala His 965 970 975
- Arg Ser Arg Tyr Val Arg Leu Arg Gln Arg Leu Cys Arg Gln Ser Val 980 985 990
- Leu Leu Trp Pro His Gln Pro Ser Gly Gln Arg Ser Phe Trp Ala Gln
 995 1000 1005
- Leu Gly Thr Ala Leu Thr Arg Asp Asn Arg His Phe Tyr Asn Gln 1010 1015 1020

Asn Phe Cys Arg Gly Pro Thr Thr Ala 1025 1030

<210> 22

<211> 822 <212> PRT <213> Canis familiaris

<400> 22

Met Gly Pro Cys Arg Gly Ala Leu His Pro Leu Ser Leu Leu Val Gln 5

Ala Ala Ala Leu Ala Leu Ala Gln Gly Thr Leu Pro Ala Phe 25

Leu Pro Cys Glu Leu Gln Pro His Gly Leu Val Asn Cys Asn Trp Leu

Phe Leu Lys Ser Val Pro Arg Phe Ser Ala Ala Ala Pro Arg Gly Asn 50 55

Val Thr Ser Leu Ser Leu Tyr Ser Asn Arg Ile His His Leu His Asp

Tyr Asp Phe Val His Phe Val His Leu Arg Arg Leu Asn Leu Lys Trp

Asn Cys Pro Pro Ala Ser Leu Ser Pro Met His Phe Pro Cys His Met 100 105 110

Thr Ile Glu Pro Asn Thr Phe Leu Ala Val Pro Thr Leu Glu Asp Leu 115 120

Asn Leu Ser Tyr Asn Ser Ile Thr Thr Val Pro Ala Leu Pro Ser Ser

Leu Val Ser Leu Ser Leu Ser Arg Thr Asn Ile Leu Val Leu Asp Pro 145 150

Ala Thr Leu Ala Gly Leu Tyr Ala Leu Arg Phe Leu Phe Leu Asp Gly 165 170

Asn Cys Tyr Tyr Lys Asn Pro Cys Gln Gln Ala Leu Gln Val Ala Pro 180 185

Gly Ala Leu Leu Gly Leu Gly Asn Leu Thr His Leu Ser Leu Lys Tyr 195 200 205

- Asn Asn Leu Thr Val Val Pro Arg Gly Leu Pro Pro Ser Leu Glu Tyr 210 215 220
- Leu Leu Ser Tyr Asn His Ile Ile Thr Leu Ala Pro Glu Asp Leu 225 230 235 240
- Ala Asn Leu Thr Ala Leu Arg Val Leu Asp Val Gly Gly Asn Cys Arg 245 250 255
- Arg Cys Asp His Ala Arg Asn Pro Cys Arg Glu Cys Pro Lys Gly Phe 260 , 265 270
- Pro Gln Leu His Pro Asn Thr Phe Gly His Leu Ser His Leu Glu Gly 275 280 285
- Leu Val Leu Arg Asp Ser Ser Leu Tyr Ser Leu Asp Pro Arg Trp Phe 290 295 300
- His Gly Leu Gly Asn Leu Met Val Leu Asp Leu Ser Glu Asn Phe Leu 305 310 315 320
- Tyr Asp Cys Ile Thr Lys Thr Lys Ala Phe Tyr Gly Leu Ala Arg Leu 325 330 335
- Arg Arg Leu Asn Leu Ser Phe Asn Tyr His Lys Lys Val Ser Phe Ala 340 345 350
- His Leu His Leu Ala Ser Ser Phe Gly Ser Leu Leu Ser Leu Gln Glu 355 360 365
- Leu Asp Ile His Gly Ile Phe Phe Arg Ser Leu Ser Lys Thr Thr Leu 370 375 380
- Gln Ser Leu Ala His Leu Pro Met Leu Gln Arg Leu His Leu Gln Leu 385 390 395 400
- Asn Phe Ile Ser Gln Ala Gln Leu Ser Ile Phe Gly Ala Phe Pro Gly 405 410 415
- Leu Arg Tyr Val Asp Leu Ser Asp Asn Arg Ile Ser Gly Ala Ala Glu
 420 425 430

Pro Ala Ala Ala Thr Gly Glu Val Glu Ala Asp Cys Gly Glu Arg Val
435 440 445

Trp Pro Gln Ser Arg Asp Leu Ala Leu Gly Pro Leu Gly Thr Pro Gly 450 455 460

Ser Glu Ala Phe Met Pro Ser Cys Arg Thr Leu Asn Phe Thr Leu Asp 465 470 475 480

Leu Ser Arg Asn Asn Leu Val Thr Val Gln Pro Glu Met Phe Val Arg 485 490 495

Leu Ala Arg Leu Gln Cys Leu Gly Leu Ser His Asn Ser Ile Ser Gln 500 505 510

Ala Val Asn Gly Ser Gln Phe Val Pro Leu Ser Asn Leu Arg Val Leu 515 520 525

Asp Leu Ser His Asn Lys Leu Asp Leu Tyr His Gly Arg Ser Phe Thr 530 540

Glu Leu Pro Arg Leu Glu Ala Leu Asp Leu Ser Tyr Asn Ser Gln Pro 545 550 555 560

Phe Ser Met Arg Gly Val Gly His Asn Leu Ser Phe Val Ala Gln Leu 565 570 575

Pro Ala Leu Arg Tyr Leu Ser Leu Ala His Asn Gly Ile His Ser Arg 580 585 590

Val Ser Gln Gln Leu Arg Ser Ala Ser Leu Arg Ala Leu Asp Phe Ser 595 600 605

Gly Asn Thr Leu Ser Gln Met Trp Ala Glu Gly Asp Leu Tyr Leu Arg 610 615 620

Phe Phe Gln Gly Leu Arg Ser Leu Val Gln Leu Asp Leu Ser Gln Asn 625 630 635 640

Arg Leu His Thr Leu Leu Pro Arg Asn Leu Asp Asn Leu Pro Lys Ser 645 650 655

Leu Arg Leu Leu Arg Leu Arg Asp Asn Tyr Leu Ala Phe Phe Asn Trp

																•
			660)				665	;				670)		
Ser	Ser	Leu 675	Ala	Leu	Leu	Pro	Lys 680	Leu	Glu	ı Ala	Leu	Asp 685		Ala	Gly	
Asn	Gln 690	Leu	Lys	Ala	Leu	Ser 695	Asn	Gly	Ser	Leu	Pro 700	Asn	Gly	Thr	Gln	
Leu 705	Gln	Arg	Leu	Asp	Leu 710	Ser	Gly	Asn	Ser	Ile 715	Gly	Phe	Val	Val	Pro 720	
Ser	Phe	Phe	Ala	Leu 725	Ala	Val	Arg	Leu	Arg 730	Glu	Leu	Asn	Leu	Ser 735	Ala	
Asn	Ala	Leu	Lys 740	Thr	Val	Glu	Pro	Ser 745	Trp	Phe	Gly	Ser	Leu 750	Ala	Gly	
Ala	Leu	Lys 755	Val	Leu	Asp	Val	Thr 760	Ala	Asn	Pro	Leu	His 765	Cys	Ala	Cys	
Gly	Ala 770	Thr	Phe	Val	Asp	Phe 775	Leu	Leu	Glu	Val	Gln 780	Ala	Ala	Val	Pro	
Gly 785	Leu	Pro	Ser	Arg	Val 790	Lys	Cys	Gly	Ser	Pro 795	Gly	Gln	Leu	Gln	Gly 800	·
Arg	Ser	Ile	Phe	Ala 805	Gln	Asp	Leu	Arg	Leu 810	Cys	Leu	Asp	Glu	Ala 815	Leu	
Ser	Trp		Суs 820	Phe	Ser											
<210: <211: <212: <213:	> 3. > Di > Ca	334 NA anis	fam	ilia	ris											
			gtga	gctc	c aa	gcate	cctt	tcc	tgca	gct (gctq	cca	ac ci	tacci	agcca	

<400> 23
aggaaggggc tgtgagctcc aagcatcett teetgeaget getgeecage ctgecageca 60
gaccetetgg agaagcecce getecetgte atgggeecet geegtggege cetgeacece 120
ctgtetetee tggtgeagge tgeegegeta geeetggeee tggeecaggg caccetgeet 180
geetteetge cetgtgaget ceagececat ggeetggtga aetgeaactg getgtteete 240
aagteegtge ceegettete ggeagetgea eecegggta aegteaceag cettteettg 300

tactccaacc gcatccacca	cctccatgac	tatgactttg	tccacttcgt	ccacctgcgg	360
cgtctcaatc tcaagtggaa	ctgcccgccc	gccagcctca	gccccatgca	ctttccctgt	420
cacatgacca ttgagcccaa	caccttcctg	gctgtgccca	ccctagagga	cctgaatctg	480
agctataaca gcatcacgac	tgtgcccgcc	ctgcccagtt	cgcttgtgtc	cctgtccctg	540
agccgcacca acatcctggt	gctggaccct	gccaccctgg	caggccttta	tgccctgcgc	600
ttcctgttcc tggatggcaa	ctgctactac	aagaacccct	gccagcaggc	cctgcaggtg	660
gccccaggtg ccctcctggg	cctgggcaac	ctcacacacc	tgtcactcaa	gtacaacaac	720
ctcaccgtgg tgccgcgggg	cctgccccc	agcctggagt	acctgctctt	gtcctacaac	780
cacatcatca ccctggcacc	tgaggacctg	gccaatctga	ctgccctgcg	tgtcctcgat	840
gtgggtggga actgtcgccg	ctgtgaccat	gcccgtaacc	cctgcaggga	gtgccccaag	900
ggcttccccc agctgcaccc	caacaccttc	ggccacctga	gccacctcga	aggcctggtg	960
ttgagggaca gctctctcta	cagcctggac	cccaggtggt	tccatggcct	gggcaacctc	1020
atggtgctgg acctgagtga	gaacttcctg	tatgactgca	tcaccaaaac	caaagccttc	1080
tacggcctgg cccggctgcg	cagactcaac	ctgtccttca	attatcataa	gaaggtgtcc	1140
tttgcccacc tgcatctggc	atcctccttc	gggagcctac	tgtccctgca	ggagctggac	1200
atacatggca tcttcttccg	ctcgctcagc	aagaccacgc	tecagteget	ggcccacctg	1260
cccatgctcc agcgtctgca	tctgcagttg	aactttatca	gccaggccca	gctcagcatc	1320
ttcggcgcct tccctggact	gcggtacgtg	gacttgtcag	acaaccgcat	cagtggagct	1380
gcagagcccg cggctgccac	aggggaggta	gaggcagact	gtggggagag	agtctggcca	1440
cagteceggg accttgetet	gggcccactg	ggcacccccg	gctcagaggc	cttcatgccg	1500
agctgcagga ccctcaactt	caccttggac	ctgtctcgga	acaacctagt	gactgttcag	1560
ccggagatgt ttgtccggct	ggcgcgcctc	cagtgcctgg	gcctgagcca	caacagcatc	1620
tegeaggegg teaatggete	gcagttcgtg	cctctgagca	acctgcgggt	gctggacctg	1680
tcccataaca agctggacct	gtaccacggg	cgctcgttca	cggagctgcc	gcggctggag	1740
gccttggacc tcagctacaa	cagccagccc	ttcagcatgc	ggggcgtggg	ccacaatctc	1800
agetttgtgg cacagetgee	agccctgcgc	tacctcagcc	tggcgcacaa	tggcatccac	1860
agccgcgtgt cccagcagct	ccgcagcgcc	tcgctccggg	ccctggactt	cagtggcaat	1920
accctgagcc agatgtgggc	cgagggagac	ctctatctcc	gcttcttcca	aggcctgaga	1980
agcctggttc agctggacct	gtcccagaat	cgcctgcata	ccctcctgcc	acgcaacctg	2040
gacaacctcc ccaagagcct	gcggctcctg	cggctccgtg	acaattacct	ggctttcttc	2100

aactggagca	gcctggccct	cctacccaag	ctggaagccc	tggacctggc	gggaaaccag	216`0
ctgaaggccc	tgagcaatgg	cagcttgccc	aacggcaccc	agctccagag	gctggacctc	2220
agcggcaaca	gcatcggctt	cgtggtcccc	agcttttttg	ccctggccgt	gaggcttcga	2280
gagctcaacc	tcagcgccaa	cgccctcaag	acggtggagc	cctcctggtt	tggttccctg	2340
gcgggtgccc	tgaaagtcct	agacgtgacc	gccaacccct	tgcattgcgc	ttgcggcgca	2400
accttcgtgg	acttcttgct	ggaggtgcag	gctgcggtgc	ccggcctgcc	tagccgtgtc	2460
aagtgcggca	gcccgggcca	gctccagggc	cgcagcatct	tcgcacagga	cctgcgcctc	2520
tgcctggacg	aagcgctctc	ctgggtctgt	ttcagcctct	cgctgctggc	tgtggccctg	2580
agectggetg	tgcccatgct	gcaccagete	tgtggctggg	acctctggta	ctgcttccac	2640
ctgtgcctgg	cctggctgcc	ccggcggggg	cggcggcggg	gtgtggatgc	cctggcctat	2700
gacgccttcg	tggtcttcga	caaggcgcag	agctcggtgg	cggactgggt	gtacaatgag	2760
ctgcgggtac	agctagagga	gcgccgtggg	cgccgggcgc	tacgcctgtg	tctggaggaa	2820
cgtgactggg	tacccggcaa	aaccctcttc	gagaacctct	gggcctcagt	ttacagcagc	2880
cgcaagacgc	tgtttgtgct	ggcccgcacg	gacagagtca	gcggcctcct	gcgtgccagc	2940
ttcctgctgg	cccaacagcg	cctgctggag	gaccgcaagg	acgtcgtggt	gctggtgatc	3000
ctgtgccccg	acgcccaccg	ctcccgctat	gtgcggctgc	gccagcgcct	ctgccgccag	3060
agtgtcctcc	tctggcccca	ccagcccagt	ggccagcgca	gcttctgggc	ccagctgggc	3120
acggccctga	ccagggacaa	ccgccacttc	tacaaccaga	acttctgccg	gggccccacg	3180
acagcctgat	aggcagacag	cccagcacct	tegegeeect	acaccctgcc	tgtctgtctg	3240
ggatgcccga	cctgctggct	ctacaccgcc	gctctgtctc	ccctacaccc	agccctggca	3300
taaagcgacc	gctcaataaa	tgctgctggt	agac			3334

<210> 24

<211> 2466

<212> DNA

<213> Canis familiaris

<400> 24

atgggccct gccgtggcgc cctgcaccc ctgtctctc tggtgcaggc tgccgcgcta 60
gccctggccc tggcccaggg caccctgcct gccttcctgc cctgtgagct ccagccccat 120
ggcctggtga actgcaactg gctgttcctc aagtccgtgc cccgcttctc ggcagctgca 180
ccccgcggta acgtcaccag cctttccttg tactccaacc gcatccacca cctccatgac 240
tatgactttg tccacttcgt ccacctgcgg cgtctcaatc tcaagtggaa ctgcccgccc 300

gccagcctca	gccccatgca	ctttccctgt	cacatgacca	ttgagcccaa	caccttcctg	360
gctgtgccca	ccctagagga	cctgaatctg	agctataaca	gcatcacgac	tgtgcccgcc	420
ctgcccagtt	cgcttgtgtc	cctgtccctg	agccgcacca	acatcctggt	gctggaccct	480
gccaccctgg	caggccttta	tgccctgcgc	ttcctgttcc	tggatggcaa	ctgctactac	540
aagaacccct	gccagcaggc	cctgcaggtg	gccccaggtg	ccctcctggg	cctgggcaac	600
ctcacacacc	tgtcactcaa	gtacaacaac	ctcaccgtgg	tgccgcgggg	cctgccccc	660
agcctggagt	acctgctctt	gtcctacaac	cacatcatca	ccctggcacc	tgaggacctg	720
gccaatctga	ctgccctgcg	tgtcctcgat	gtgggtggga	actgtcgccg	ctgtgaccat	780
gcccgtaacc	cctgcaggga	gtgccccaag	ggcttccccc	agctgcaccc	caacaccttc	840
ggccacctga	gccacctcga	aggcctggtg	ttgagggaca	gctctctcta	cagcctggac	900
cccaggtggt	tccatggcct	gggcaacctc	atggtgctgg	acctgagtga	gaacttcctg	960
tatgactgca	tcaccaaaac	caaagccttc	tacggcctgg	cccggctgcg	cagactcaac	1020
ctgtccttca	attatcataa	gaaggtgtcc	tttgcccacc	tgcatctggc	atcctccttc	1080
gggagcctac	tgtccctgca	ggagctggac	atacatggca	tcttcttccg	ctcgctcagc	1140
aagaccacgc	tccagtcgct	ggcccacctg	cccatgctcc	agcgtctgca	tctgcagttg	1200
aactttatca	gccaggccca	gctcagcatc	ttcggcgcct	tccctggact	gcggtacgtg	1260
gacttgtcag	acaaccgcat	cagtggagct	gcagagcccg	cggctgccac	aggggaggta	1320
gaggcagact	gtggggagag	ągtctggcca	cagtcccggg	accttgctct	gggcccactg	1380
ggcacccccg	gctcagaggc	cttcatgccg	agctgcagga	ccctcaactt	caccttggac	1440
ctgtctcgga	acaacctagt	gactgttcag	ccggagatgt	ttgtccggct	ggcgcgcctc	1500
cagtgcctgg	gcctgagcca	caacagcatc	tcgcaggcgg	tcaatggctc	gcagttcgtg	1560
cctctgagca	acctgcgggt	gctggacctg	tcccataaca	agctggacct	gtaccacggg	1620
cgctcgttca	cggagctgcc	gcggctggag	gccttggacc	tcagctacaa	cagccagccc	1680
ttcagcatgc	ggggcgtggg	ccacaatctc	agctttgtgg	cacagctgcc	agccctgcgc	1740
tacctcagcc	tggcgcacaa	tggcatccac	agccgcgtgt	cccagcagct	ccgcagcgcc	1800
tegeteeggg	ccctggactt	cagtggcaat	accctgagcc	agatgtgggc	cgagggagac	1860
ctctatctcc	gcttcttcca	aggcctgaga	agcctggttc	agctggacct	gtcccagaat	1920
cgcctgcata	ccctcctgcc	acgcaacctg	gacaacctcc	ccaagagcct	gcggctcctg	1980
cggctccgtg	acaattacct	ggctttcttc	aactggagca	gcctggccct	cctacccaag	2040

ctggaago	cc tggacctggc	gggaaaccag	ctgaaggccc	tgagcaatgg	cagcttgccc	2100
aacggcac	cc agctccagag	gctggacctc	agcggcaaca	gcatcggctt	cgtggtcccc	2160
agcttttt	tg ccctggccgt	gaggcttcga	gagctcaacc	tcagcgccaa	cgccctcaag	2220
acggtgga	gc cctcctggtt	tggttccctg	gcgggtgccc	tgaaagtcct	agacgtgacc	2280
gccaacco	ct tgcattgcgc	ttgcggcgca	accttcgtgg	acttcttgct	ggaggtgcag	2340
gctgcggt	gc ccggcctgcc	tagccgtgtc	aagtgcggca	gcccgggcca	gctccagggc	2400
cgcagcat	ct tcgcacagga	cctgcgcctc	tgcctggacg	aagcgctctc	ctgggtctgt	2460
ttcagc						2466

<210> 25

<211> 1031

<212> PRT

<213> Felis catus

<400> 25

Met Gly Pro Cys His Gly Ala Leu His Pro Leu Ser Leu Leu Val Gln 1 5 10 10

Ala Ala Ala Leu Ala Val Ala Leu Ala Gln Gly Thr Leu Pro Ala Phe 20 25 30

Leu Pro Cys Glu Leu Gln Arg His Gly Leu Val Asn Cys Asp Trp Leu 35 40 45

Phe Leu Lys Ser Val Pro His Phe Ser Ala Ala Ala Pro Arg Gly Asn 50 55 60

Val Thr Ser Leu Ser Leu Tyr Ser Asn Arg Ile His His Leu His Asp 65 70 75 80

Ser Asp Phe Val His Leu Ser Ser Leu Arg Arg Leu Asn Leu Lys Trp 85 90 95

Asn Cys Pro Pro Ala Ser Leu Ser Pro Met His Phe Pro Cys His Met 100 105 110

Thr Ile Glu Pro His Thr Phe Leu Ala Val Pro Thr Leu Glu Glu Leu 115 120 125

Asn Leu Ser Tyr Asn Ser Ile Thr Thr Val Pro Ala Leu Pro Ser Ser 130 135 140

Leu Val Ser Leu Ser Leu Ser Arg Thr Asn Ile Leu Val Leu Asp Pro 145 150 155 160

- Ala Asn Leu Ala Gly Leu His Ser Leu Arg Phe Leu Phe Leu Asp Gly 165 170 175
- Asn Cys Tyr Tyr Lys Asn Pro Cys Pro Gln Ala Leu Gln Val Ala Pro 180 185 190
- Gly Ala Leu Leu Gly Leu Gly Asn Leu Thr His Leu Ser Leu Lys Tyr 195 200 205
- Asn Asn Leu Thr Ala Val Pro Arg Gly Leu Pro Pro Ser Leu Glu Tyr 210 215 220
- Leu Leu Ser Tyr Asn His Ile Ile Thr Leu Ala Pro Glu Asp Leu 225 230 235 240
- Ala Asn Leu Thr Ala Leu Arg Val Leu Asp Val Gly Gly Asn Cys Arg 245 250 255
- Arg Cys Asp His Ala Arg Asn Pro Cys Met Glu Cys Pro Lys Gly Phe 260 265 270
- Pro His Leu His Pro Asp Thr Phe Ser His Leu Asn His Leu Glu Gly
 275 280 285
- Leu Val Leu Lys Asp Ser Ser Leu Tyr Asn Leu Asn Pro Arg Trp Phe 290 295 300
- His Ala Leu Gly Asn Leu Met Val Leu Asp Leu Ser Glu Asn Phe Leu 305 310 315 320
- Tyr Asp Cys Ile Thr Lys Thr Thr Ala Phe Gln Gly Leu Ala Gln Leu 325 330 335
- Arg Arg Leu Asn Leu Ser Phe Asn Tyr His Lys Lys Val Ser Phe Ala 340 345 350
- His Leu His Leu Ala Pro Ser Phe Gly Ser Leu Leu Ser Leu Gln Gln 355 360 365
- Leu Asp Met His Gly Ile Phe Phe Arg Ser Leu Ser Glu Thr Thr Leu 370 375 380

Arg Ser Leu Val His Leu Pro Met Leu Gln Ser Leu His Leu Gln Met 385

- Asn Phe Ile Asn Gln Ala Gln Leu Ser Ile Phe Gly Ala Phe Pro Gly 405 410 415
- Leu Arg Tyr Val Asp Leu Ser Asp Asn Arg Ile Ser Gly Ala Met Glu
 420 425 430
- Leu Ala Ala Thr Gly Glu Val Asp Gly Gly Glu Arg Val Arg Leu
 435 440 445
- Pro Ser Gly Asp Leu Ala Leu Gly Pro Pro Gly Thr Pro Ser Ser Glu 450 455 460
- Gly Phe Met Pro Gly Cys Lys Thr Leu Asn Phe Thr Leu Asp Leu Ser 470 475 480
- Arg Asn Asn Leu Val Thr Ile Gln Pro Glu Met Phe Ala Arg Leu Ser 485 490 495
- Arg Leu Gln Cys Leu Leu Leu Ser Arg Asn Ser Ile Ser Gln Ala Val
 500 505 510
- Asn Gly Ser Gln Phe Met Pro Leu Thr Ser Leu Gln Val Leu Asp Leu 515 520 525
- Ser His Asn Lys Leu Asp Leu Tyr His Gly Arg Ser Phe Thr Glu Leu 530 540
- Pro Arg Leu Glu Ala Leu Asp Leu Ser Tyr Asn Ser Gln Pro Phe Ser 545 550 555 560
- Met Gln Gly Val Gly His Asn Leu Ser Phe Val Ala Gln Leu Pro Ala 565 570 575
- Leu Arg Tyr Leu Ser Leu Ala His Asn Asp Ile His Ser Arg Val Ser 580 585 590
- Gln Gln Leu Cys Ser Ala Ser Leu Arg Ala Leu Asp Phe Ser Gly Asn 595 600 605
- Ala Leu Ser Arg Met Trp Ala Glu Gly Asp Leu Tyr Leu His Phe Phe

610 615 620

Arg Gly Leu Arg Ser Leu Val Arg Leu Asp Leu Ser Gln Asn Arg Leu 625 630 635 640

His Thr Leu Leu Pro Arg Thr Leu Asp Asn Leu Pro Lys Ser Leu Arg 645 650 655

Leu Leu Arg Leu Arg Asp Asn Tyr Leu Ala Phe Phe Asn Trp Ser Ser 660 665 670

Leu Val Leu Leu Pro Arg Leu Glu Ala Leu Asp Leu Ala Gly Asn Gln 675 680 685

Leu Lys Ala Leu Ser Asn Gly Ser Leu Pro Asn Gly Thr Gln Leu Gln 690 695 700

Arg Leu Asp Leu Ser Ser Asn Ser Ile Ser Phe Val Ala Ser Ser Phe 705 710 715 720

Phe Ala Leu Ala Thr Arg Leu Arg Glu Leu Asn Leu Ser Ala Asn Ala 725 730 735

Leu Lys Thr Val Glu Pro Ser Trp Phe Gly Ser Leu Ala Gly Thr Leu 740 745 750

Lys Val Leu Asp Val Thr Gly Asn Pro Leu His Cys Ala Cys Gly Ala
755 760 765

Ala Phe Val Asp Phe Leu Leu Glu Val Gln Ala Ala Val Pro Gly Leu 770 780

Pro Gly His Val Lys Cys Gly Ser Pro Gly Gln Leu Gln Gly Arg Ser 785 790 795 . 800

Ile Phe Ala Gln Asp Leu Arg Leu Cys Leu Asp Glu Ala Leu Ser Trp 805 810 815

Asp Cys Phe Gly Leu Ser Leu Leu Thr Val Ala Leu Gly Leu Ala Val 820 825 830

Pro Met Leu His His Leu Cys Gly Trp Asp Leu Trp Tyr Cys Phe His 835 840 845

Leu Cys Leu Ala Trp Leu Pro Arg Arg Gly Arg Arg Gly Ala Asp 850

Ala Leu Pro Tyr Asp Ala Phe Val Val Phe Asp Lys Ala Gln Ser Ala 870 875

Val Ala Asp Trp Val Tyr Asn Glu Leu Arg Val Arg Leu Glu Glu Arg 885 890

Arg Gly Arg Arg Ala Leu Arg Leu Cys Leu Glu Glu Arg Asp Trp Leu 900 905

Pro Gly Lys Thr Leu Phe Glu Asn Leu Trp Ala Ser Val Tyr Ser Ser 915 920 925

Arg Lys Met Leu Phe Val Leu Ala His Thr Asp Arg Val Ser Gly Leu 930 935

Leu Arg Ala Ser Phe Leu Leu Ala Gln Gln Arg Leu Leu Glu Asp Arg 945 955

Lys Asp Val Val Leu Val Ile Leu Arg Pro Asp Ala His Arg Ser 965 975

Arg Tyr Val Arg Leu Arg Gln Arg Leu Cys Arg Gln Ser Val Leu Leu 980 985

Trp Pro His Gln Pro Ser Gly Gln Arg Ser Phe Trp Ala Gln Leu Gly 995 1000

Thr Ala Leu Thr Arg Asp Asn Gln His Phe Tyr Asn Gln Asn Phe 1010 1015 1020

Cys Arg Gly Pro Thr Thr Ala Glu 1025 1030

<210> 26 <211> 820 <212> PRT

<213> Felis catus

<400> 26

Met Gly Pro Cys His Gly Ala Leu His Pro Leu Ser Leu Leu Val Gln 5 10

Ala Ala Leu Ala Val Ala Leu Ala Gln Gly Thr Leu Pro Ala Phe 20 25 30

- Leu Pro Cys Glu Leu Gln Arg His Gly Leu Val Asn Cys Asp Trp Leu 35 40
- Phe Leu Lys Ser Val Pro His Phe Ser Ala Ala Pro Arg Gly Asn 50 55
- Val Thr Ser Leu Ser Leu Tyr Ser Asn Arg Ile His His Leu His Asp
 65 70 75 80
- Ser Asp Phe Val His Leu Ser Ser Leu Arg Arg Leu Asn Leu Lys Trp 85 90 95
- Asn Cys Pro Pro Ala Ser Leu Ser Pro Met His Phe Pro Cys His Met 100 105 110
- Thr Ile Glu Pro His Thr Phe Leu Ala Val Pro Thr Leu Glu Glu Leu 115 120 125
- Asn Leu Ser Tyr Asn Ser Ile Thr Thr Val Pro Ala Leu Pro Ser Ser 130 140
- Leu Val Ser Leu Ser Leu Ser Arg Thr Asn Ile Leu Val Leu Asp Pro 145 150 155 160
- Ala Asn Leu Ala Gly Leu His Ser Leu Arg Phe Leu Phe Leu Asp Gly 165 170 175
- Asn Cys Tyr Tyr Lys Asn Pro Cys Pro Gln Ala Leu Gln Val Ala Pro 180 185 190
- Gly Ala Leu Leu Gly Leu Gly Asn Leu Thr His Leu Ser Leu Lys Tyr 195 200 205
- Asn Asn Leu Thr Ala Val Pro Arg Gly Leu Pro Pro Ser Leu Glu Tyr 210 215 220
- Leu Leu Ser Tyr Asn His Ile Ile Thr Leu Ala Pro Glu Asp Leu 225 235 240
- Ala Asn Leu Thr Ala Leu Arg Val Leu Asp Val Gly Gly Asn Cys Arg 245 250 255

Arg Cys Asp His Ala Arg Asn Pro Cys Met Glu Cys Pro Lys Gly Phe 260 265 270

- Pro His Leu His Pro Asp Thr Phe Ser His Leu Asn His Leu Glu Gly 275 280 285
- Leu Val Leu Lys Asp Ser Ser Leu Tyr Asn Leu Asn Pro Arg Trp Phe 290 295 300
- His Ala Leu Gly Asn Leu Met Val Leu Asp Leu Ser Glu Asn Phe Leu 305 310 315 320
- Tyr Asp Cys Ile Thr Lys Thr Thr Ala Phe Gln Gly Leu Ala Gln Leu 325 330 335
- Arg Arg Leu Asn Leu Ser Phe Asn Tyr His Lys Lys Val Ser Phe Ala 340 345 350
- His Leu His Leu Ala Pro Ser Phe Gly Ser Leu Leu Ser Leu Gln Gln 355 360 365
- Leu Asp Met His Gly Ile Phe Phe Arg Ser Leu Ser Glu Thr Thr Leu 370 380
- Arg Ser Leu Val His Leu Pro Met Leu Gln Ser Leu His Leu Gln Met 385 390 395 400
- Asn Phe Ile Asn Gln Ala Gln Leu Ser Ile Phe Gly Ala Phe Pro Gly 405 410 415
- Leu Arg Tyr Val Asp Leu Ser Asp Asn Arg Ile Ser Gly Ala Met Glu 420 425 430
- Leu Ala Ala Thr Gly Glu Val Asp Gly Gly Glu Arg Val Arg Leu 435 440 445
- Pro Ser Gly Asp Leu Ala Leu Gly Pro Pro Gly Thr Pro Ser Ser Glu 450 455 460
- Gly Phe Met Pro Gly Cys Lys Thr Leu Asn Phe Thr Leu Asp Leu Ser 470 475 480
- Arg Asn Asn Leu Val Thr Ile Gln Pro Glu Met Phe Ala Arg Leu Ser 485 490 495

Arg Leu Gln Cys Leu Leu Ser Arg Asn Ser Ile Ser Gln Ala Val 500 505 510

- Asn Gly Ser Gln Phe Met Pro Leu Thr Ser Leu Gln Val Leu Asp Leu 515 520 525
- Ser His Asn Lys Leu Asp Leu Tyr His Gly Arg Ser Phe Thr Glu Leu 530 535 540
- Pro Arg Leu Glu Ala Leu Asp Leu Ser Tyr Asn Ser Gln Pro Phe Ser 545 550 555 560
- Met Gln Gly Val Gly His Asn Leu Ser Phe Val Ala Gln Leu Pro Ala 565 570 575
- Leu Arg Tyr Leu Ser Leu Ala His Asn Asp Ile His Ser Arg Val Ser 580 585 590
- Gln Gln Leu Cys Ser Ala Ser Leu Arg Ala Leu Asp Phe Ser Gly Asn 595 600 605
- Ala Leu Ser Arg Met Trp Ala Glu Gly Asp Leu Tyr Leu His Phe Phe 610 615 620
- Arg Gly Leu Arg Ser Leu Val Arg Leu Asp Leu Ser Gln Asn Arg Leu 625 630 635
- His Thr Leu Leu Pro Arg Thr Leu Asp Asn Leu Pro Lys Ser Leu Arg 645 650 655
- Leu Leu Arg Leu Arg Asp Asn Tyr Leu Ala Phe Phe Asn Trp Ser Ser 660 665 670
- Leu Val Leu Leu Pro Arg Leu Glu Ala Leu Asp Leu Ala Gly Asn Gln 675 680 685
- Leu Lys Ala Leu Ser Asn Gly Ser Leu Pro Asn Gly Thr Gln Leu Gln 690 695 700
- Arg Leu Asp Leu Ser Ser Asn Ser Ile Ser Phe Val Ala Ser Ser Phe 705 710 715 720
- Phe Ala Leu Ala Thr Arg Leu Arg Glu Leu Asn Leu Ser Ala Asn Ala

725 730 735

Leu Lys Thr Val Glu Pro Ser Trp Phe Gly Ser Leu Ala Gly Thr Leu 740 745 750

Lys Val Leu Asp Val Thr Gly Asn Pro Leu His Cys Ala Cys Gly Ala 755 760 765

Ala Phe Val Asp Phe Leu Leu Glu Val Gln Ala Ala Val Pro Gly Leu 770 780

Pro Gly His Val Lys Cys Gly Ser Pro Gly Gln Leu Gln Gly Arg Ser 785 790 795 800

Ile Phe Ala Gln Asp Leu Arg Leu Cys Leu Asp Glu Ala Leu Ser Trp 805 810 815

Asp Cys Phe Gly 820

<210> 27

<211> 3235

<212> DNA

<213> Felis catus

<400> 27

agggtetgeg agetecagge attettetet gecategetg cecagtetge catecagace 60 ctctggagaa gececcaete cetgtcatgg gecectgeca tggegeeetg caceccetgt 120 ctctcctggt gcaggctgcc gcgctggccg tggccctggc ccagggcacc ctgcctgcct 180 ttetgeeetg tgageteeag egeeaeggee tggtgaattg egaetggetg tteeteaagt 240 ccgtgcccca cttctcggcg gcagcgcccc gtggtaacgt caccagcctt tccctgtact 300 ccaaccgcat ccaccacctc cacgactecg actttgtcca cctgtccagc ctgcggcgtc 360 tcaacctcaa atggaactgc ccacccgcca gcctcagccc catgcacttc ccctgtcaca 420 tgaccattga gccccacacc ttcctggccg tgcccaccct ggaggagctg aacctgagct 480 acaacagcat cacgacagta cccgccctgc ccagttccct cgtgtccctg tccttgagcc 540 gtaccaacat cetggtgetg gaccetgeca acetegeagg getgeactee etgegettte 600 tgttcctgga tggcaactgc tactacaaga acccctgccc gcaggccctg caggtggccc 660 egggegeect cettggeetg ggcaacetta egcaeetgte acteaagtae aacaacetea 720 ctgcggtgcc ccgcggcctg cccccagcc tggagtacct gctattgtcc tacaaccaca 780

tcatcaccct	ggcacctgag	gacctggcca	acctgaccgc	cctgcgtgtg	ctcgatgtgg	840
gtgggaactg	ccgtcgctgt	gaccacgccc	gcaacccctg	tatggagtgc	cccaagggct	900
tcccgcacct	gcaccctgac	accttcagcc	acctgaacca	cctcgaaggc	ctggtgttga	960
aggacagctc	tctctacaac	ctgaacccca	gatggttcca	tgccctgggc	aacctcatgg	1020
tgctggacct	gagtgagaac	ttcctatatg	actgcatcac	caaaaccaca	gccttccagg	1080
gcctggccca	gctgcgcaga	ctcaacttgt	ctttcaatta	ccacaagaag	gtgtcctttg	1140
cccacctgca	tetggegeee	tccttcggga	gcctgctctc	cctgcagcag	ctggacatgc	1200
atggcatctt	cttccgctcg	ctcagcgaga	ccacgetccg	gtcgctggtc	cacctgccca	1260
tgctccagag	tctgcacctg	cagatgaact	tcatcaatca	ggcccagctc	agcatcttcg	1320
gggccttccc	tggcctgcga	tacgtggacc	tgtcagacaa	ccgcataagt	ggagccatgg	1380
agctggcggc	tgccacgggg	gaggtggatg	gtggggagag	agtccggctg	ccatctgggg	1440
acctagctct	gggcccaccg	ggcaccccta	gctccgaggg	cttcatgcca	ggctgcaaga	1500
ccctcaactt	caccttggac	ctgtcacgga	acaacctagt	gacaatccag	ccagagatgt	1560
ttgcccggct	ctcgcgcctc	cagtgcctgc	tcctgagccg	caacagcatc	tegeaggeag	1620
tcaacggctc	acaatttatg	ccgctgacca	gcctgcaggt	gctggacctg	tcccataaca	1680
agctggacct	gtaccatggg	cgctctttca	cggagctgcc	gcggctggag	gccctggacc	1740
tcagctacaa	cagccagccc	ttcagcatgc	agggcgtggg	tcacaacctc	agctttgtgg	1800
cacagetgee	ggccctgcgc	tatctcagcc	tggcgcacaa	cgacatccac	agccgtgtgt	1860
cccagcagct	ctgcagcgcc	tcgctgcggg	ccttggactt	cagcggcaat	gccttgagcc	1920
ggatgtggg	cgagggagac	ctgtatctcc	acttcttccg	aggcctgagg	agcctggtcc	1980
ggttggatct	gtcccagaat	cgcctgcata	ccctcttgcc	acgcaccctg	gacaacctcc	2040
ccaagagcct	geggetgetg	cgtctccgtg	acaattatct	ggctttcttc	aactggagca	2100
gcctggtcct	cctccccagg	ctggaagccc	tggacctggc	gggaaaccag	ctgaaggccc	2160
tgagcaacgg	cagettgeet	aatggaaccc	agctccagag	gctggacctc	agcagcaaca	2220
gtatcagctt	cgtggcctcc	agctttttg	ctctggccac	caggetgega	gageteaace	2280
tcagtgccaa	cgccctcaag	acggtggagc	cctcctggtt	cggttctcta	gegggeacce	2340
tgaaagtcct	agatgtgact	ggcaaccccc	tgcactgcgc	ctgtggggcg	gccttcgtgg	2400
acttcttgct	ggaggtgcag	gctgcagtgc	ccggcctgcc	aggccacgtc	aagtgtggca	2460
gtccaggtca	getecaggge	cgcagcatct	ttgcgcagga	tetgegeete	tgcctggatg	2520
aggccctctc	: ctgggactgt	tttggcctct	cgctgctgac	cgtggccctg	ggcctggccg	2580

. 15

tgcccatgct gcaccacctc tgtggctggg acctctggta ctgcttccac ctgtgcctgg 2640 cctggctgcc ccggcggggg cggcggcggg gcgcggatgc cctgccctac gatgcctttg 2700 tggtcttcga caaggcacag agcgcggtgg ccgactgggt gtacaacgag ctgcgggtac 2760 ggctagagga gcgccgtgga cgccgagcgc tccgcctgtg cctggaggaa cgtgactggc 2820 tacccggtaa aacgctcttt gagaacctgt gggcctcagt ttacagcagc cgcaagatgc 2880 tgtttgtgct ggcccacaca gacagggtca gcggcctctt gcgcgccagc tttctgctgg 2940 cccagcageg cctgctggag gaccgcaagg acgttgtggt gctggtgatc ctgcgcccg 3000 acgcccaccg ctcccgctat gtgcggctgc gccagcgcct ctgccgccag agcgtcctcc 3060 totggcccca ccagcccagt ggccagcgca gcttctgggc ccagctgggc acggccctga 3120 ccagggacaa ccagcacttc tataaccaga acttctgccg gggccccacg acggcagagt 3180 gaccgcccag caccccaagc ctcctacacc ttgcctgtct gcctgggatg ccggg 3235 <210> 28 <211> 2460 <212> DNA <213> Felis catus <400> 28 atgggcccct gccatggcgc cctgcacccc ctgtctctcc tggtgcaggc tgccgcgctg 60 gccgtggccc tggcccaggg caccctgcct gcctttctgc cctgtgagct ccagcgccac 120 ggcctggtga attgcgactg gctgttcctc aagtccgtgc cccacttctc ggcggcagcg 180 ccccgtggta acgtcaccag cctttccctg tactccaacc gcatccacca cctccacgac 240 tecgaetttg tecacetgte cageetgegg egteteaace teaaatggaa etgeceacee 300 gccagcctca gccccatgca cttcccctgt cacatgacca ttgagcccca caccttcctg 360 geegtgeeca ecctggagga getgaacetg agetacaaca geatcaegae agtaceegee 420 ctgcccagtt ccctcgtgtc cctgtccttg agccgtacca acatcctggt gctggaccct 480 gccaacctcg cagggctgca ctccctgcgc tttctgttcc tggatggcaa ctgctactac 540 aagaacccct gcccgcaggc cctgcaggtg gccccgggcg ccctccttgg cctgggcaac 600 cttacgcacc tgtcactcaa gtacaacaac ctcactgcgg tgccccgcgg cctgccccc 660 agectggagt acctgctatt gtcctacaac cacatcatca ccctggcacc tgaggacctg 720 gecaacetga cegecetgeg tgtgetegat gtgggtggga actgeegteg etgtgaceae 780 georgeaace cetgtatgga gtgccccaag ggcttcccgc acctgcaccc tgacaccttc 840

900

agecaectga accaectega aggeetggtg ttgaaggaca geteteteta caacetgaac

cccagatggt	tccatgccct	gggcaacctc	atggtgctgg	acctgagtga	gaacttccta	960
tatgactgca	tcaccaaaac	cacagccttc	cagggcctgg	cccagetgeg	cagactcaac	1020
ttgtctttca	attaccacaa	gaaggtgtcc	tttgcccacc	tgcatctggc	gccctccttc	1080
gggagcctgc	tctccctgca	gcagctggac	atgcatggca	tcttcttccg	ctcgctcagc	1140
gagaccacgc	tccggtcgct	ggtccacctg	cccatgctcc	agagtetgea	cctgcagatg	1200
aacttcatca	atcaggccca	gctcagcatc	ttcggggcct	tccctggcct	gcgatacgtg	1260
gacctgtcag	acaaccgcat	aagtggagcc	atggagctgg	cggctgccac	gggggaggtg	1320
gatggtgggg	agagagtccg	gctgccatct	ggggacctag	ctctgggccc	accgggcacc	1380
cctagctccg	agggcttcat	gccaggctgc	aagaccctca	acțtcacctt	ggacctgtca	1440
cggaacaacc	tagtgacaat	ccagccagag	atgtttgccc	ggctctcgcg	cctccagtgc	1500
ctgctcctga	gccgcaacag	catctcgcag	gcagtcaacg	gctcacaatt	tatgccgctg	1560
accagcctgc	aggtgctgga	cctgtcccat	aacaagctgg	acctgtacca	tgggcgctct	1620
ttcacggagc	tgccgcggct	ggaggccctg	gacctcagct	acaacagcca	gcccttcagc	1680
atgcagggcg	tgggtcacaa	cctcagcttt	gtggcacagc	tgccggccct	gcgctatctc	1740
agcctggcgc	acaacgacat	ccacagccgt	gtgtcccagc	agctctgcag	cgcctcgctg	1800
cgggccttgg	acttcagcgg	caatgccttg	agccggatgt	gggccgaggg	agacctgtat	1860
ctccacttct	tccgaggcct	gaggagcctg	gtccggttgg	atctgtccca	gaatcgcctg	1920
cataccctct	tgccacgcac	cctggacaac	ctccccaaga	gcctgcggct	gctgcgtctc	1980
cgtgacaatt	atctggcttt	cttcaactgg	agcagcctgg	tcctcctccc	caggctggaa	2040
gccctggacc	tggcgggaaa	ccagctgaag	gccctgagca	acggcagctt	gcctaatgga	2100
acccagetee	agaggctgga	cctcagcagç	aacagtatca	gcttcgtggc	ctccagcttt	2160
tttgctctgg	ccaccaggct	gcgagagctc	aacctcagtg	ccaacgccct	caagacggtg	2220
gagccctcct	ggttcggttc	tctagcgggc	accctgaaag	tcctagatgt	gactggcaac	2280
cccctgcact	gcgcctgtgg	ggcggccttc	gtggacttct	tgctggaggt	gcaggctgca	2340
gtgcccggcc	tgccaggcca	cgtcaagtgt	ggcagtccag	gtcagctcca	gggccgcagc	2400
atctttgcgc	aggatctgcg	cctctgcctg	gatgaggccc	tctcctggga	ctgttttggc	2460

<210> 29 .

<211> 1032

<212> PRT

<213> Mus musculus

<400> 29

Met Val Leu Arg Arg Arg Thr Leu His Pro Leu Ser Leu Leu Val Gln
1 5 10 15

Ala Ala Val Leu Ala Glu Thr Leu Ala Leu Gly Thr Leu Pro Ala Phe 20 25 30

Leu Pro Cys Glu Leu Lys Pro His Gly Leu Val Asp Cys Asn Trp Leu 35 40 45

Phe Leu Lys Ser Val Pro Arg Phe Ser Ala Ala Ala Ser Cys Ser Asn 50 55 60

Ile Thr Arg Leu Ser Leu Ile Ser Asn Arg Ile His His Leu His Asn 65 70 75 80

Ser Asp Phe Val His Leu Ser Asn Leu Arg Gln Leu Asn Leu Lys Trp 85 90 95

Asn Cys Pro Pro Thr Gly Leu Ser Pro Leu His Phe Ser Cys His Met 100 105 110

Thr Ile Glu Pro Arg Thr Phe Leu Ala Met Arg Thr Leu Glu Glu Leu 115 120 125

Asn Leu Ser Tyr Asn Gly Ile Thr Thr Val Pro Arg Leu Pro Ser Ser 130 135 140

Leu Val Asn Leu Ser Leu Ser His Thr Asn Ile Leu Val Leu Asp Ala 145 150 155 160

Asn Ser Leu Ala Gly Leu Tyr Ser Leu Arg Val Leu Phe Met Asp Gly 165 170 175

Asn Cys Tyr Tyr Lys Asn Pro Cys Thr Gly Ala Val Lys Val Thr Pro 180 185 190

Gly Ala Leu Leu Gly Leu Ser Asn Leu Thr His Leu Ser Leu Lys Tyr 195 200 205

Asn Asn Leu Thr Lys Val Pro Arg Gln Leu Pro Pro Ser Leu Glu Tyr 210 215 220

Leu Leu Val Ser Tyr Asn Leu Ile Val Lys Leu Gly Pro Glu Asp Leu

225 230 235 240

Ala Asn Leu Thr Ser Leu Arg Val Leu Asp Val Gly Gly Asn Cys Arg 245 250 255

Arg Cys Asp His Ala Pro Asn Pro Cys Ile Glu Cys Gly Gln Lys Ser 260 265 270

Leu His Leu His Pro Glu Thr Phe His His Leu Ser His Leu Glu Gly 275 280 285

Leu Val Leu Lys Asp Ser Ser Leu His Thr Leu Asn Ser Ser Trp Phe 290 295 300

Gln Gly Leu Val Asn Leu Ser Val Leu Asp Leu Ser Glu Asn Phe Leu 305 310 315 320

Tyr Glu Ser Ile Asn His Thr Asn Ala Phe Gln Asn Leu Thr Arg Leu 325 330 335

Arg Lys Leu Asn Leu Ser Phe Asn Tyr Arg Lys Lys Val Ser Phe Ala 340 345 350

Arg Leu His Leu Ala Ser Ser Phe Lys Asn Leu Val Ser Leu Gln Glu 355 360 365

Leu Asn Met Asn Gly Ile Phe Phe Arg Ser Leu Asn Lys Tyr Thr Leu 370 375 380

Arg Trp Leu Ala Asp Leu Pro Lys Leu His Thr Leu His Leu Gln Met 385 390 395 400

Leu Arg Phe Val Asp Leu Ser Asp Asn Arg Ile Ser Gly Pro Ser Thr. 420 425 430

Leu Ser Glu Ala Thr Pro Glu Glu Ala Asp Asp Ala Glu Glu Glu 435 440 445

Leu Leu Ser Ala Asp Pro His Pro Ala Pro Leu Ser Thr Pro Ala Ser 450 455 460

Lys Asn Phe Met Asp Arg Cys Lys Asn Phe Lys Phe Thr Met Asp Leu 465 470 475 480

- Ser Arg Asn Asn Leu Val Thr Ile Lys Pro Glu Met Phe Val Asn Leu 485 490 495
- Ser Arg Leu Gln Cys Leu Ser Leu Ser His Asn Ser Ile Ala Gln Ala 500 505 510
- Val Asn Gly Ser Gln Phe Leu Pro Leu Thr Asn Leu Gln Val Leu Asp 515 520 525
- Leu Ser His Asn Lys Leu Asp Leu Tyr His Trp Lys Ser Phe Ser Glu 530 535 540
- Leu Pro Gln Leu Gln Ala Leu Asp Leu Ser Tyr Asn Ser Gln Pro Phe 545 550 560
- Ser Met Lys Gly Ile Gly His Asn Phe Ser Phe Val Ala His Leu Ser 565 570 575
- Met Leu His Ser Leu Ser Leu Ala His Asn Asp Ile His Thr Arg Val 580 585 590
- Ser Ser His Leu Asn Ser Asn Ser Val Arg Phe Leu Asp Phe Ser Gly 595 600 605
- Asn Gly Met Gly Arg Met Trp Asp Glu Gly Gly Leu Tyr Leu His Phe 610 620
- Phe Gln Gly Leu Ser Gly Leu Leu Lys Leu Asp Leu Ser Gln Asn Asn 625 630 635 640
- Leu His Ile Leu Arg Pro Gln Asn Leu Asp Asn Leu Pro Lys Ser Leu 645 650 655
- Lys Leu Leu Ser Leu Arg Asp Asn Tyr Leu Ser Phe Phe Asn Trp Thr 660 665 670
- Ser Leu Ser Phe Leu Pro Asn Leu Glu Val Leu Asp Leu Ala Gly Asn 675 680 685
- Gln Leu Lys Ala Leu Thr Asn Gly Thr Leu Pro Asn Gly Thr Leu Leu 690 695 700

Gln Lys Leu Asp Val Ser Ser Asn Ser Ile Val Ser Val Val Pro Ala 705 710 715 720

Phe Phe Ala Leu Ala Val Glu Leu Lys Glu Val Asn Leu Ser His Asn 725 730 735

Ile Leu Lys Thr Val Asp Arg Ser Trp Phe Gly Pro Ile Val Met Asn 740 745 750

Leu Thr Val Leu Asp Val Arg Ser Asn Pro Leu His Cys Ala Cys Gly
755 760 765

Ala Ala Phe Val Asp Leu Leu Glu Val Gln Thr Lys Val Pro Gly 770 780

Leu Ala Asn Gly Val Lys Cys Gly Ser Pro Gly Gln Leu Gln Gly Arg
785 790 795 800

Ser Ile Phe Ala Gln Asp Leu Arg Leu Cys Leu Asp Glu Val Leu Ser 805 810 815

Trp Asp Cys Phe Gly Leu Ser Leu Leu Ala Val Ala Val Gly Met Val 820 825 830

Val Pro Ile Leu His His Leu Cys Gly Trp Asp Val Trp Tyr Cys Phe 835 840 845

His Leu Cys Leu Ala Trp Leu Pro Leu Leu Ala Arg Ser Arg Arg Ser 850 860

Ala Gln Ala Leu Pro Tyr Asp Ala Phe Val Val Phe Asp Lys Ala Gln 865 870 875 880

Ser Ala Val Ala Asp Trp Val Tyr Asn Glu Leu Arg Val Arg Leu Glu 885 890 895

Glu Arg Arg Gly Arg Arg Ala Leu Arg Leu Cys Leu Glu Asp Arg Asp 900 905 910

Trp Leu Pro Gly Gln Thr Leu Phe Glu Asn Leu Trp Ala Ser Ile Tyr 915 920 925

Gly Ser Arg Lys Thr Leu Phe Val Leu Ala His Thr Asp Arg Val Ser 930 935 940

Gly Leu Leu Arg Thr Ser Phe Leu Leu Ala Gln Gln Arg Leu Leu Glu 945 950 955 960

Asp Arg Lys Asp Val Val Leu Val Ile Leu Arg Pro Asp Ala His 965 970 975

Arg Ser Arg Tyr Val Arg Leu Arg Gln Arg Leu Cys Arg Gln Ser Val 980 985 990

Leu Phe Trp Pro Gln Gln Pro Asn Gly Gln Gly Gly Phe Trp Ala Gln 995 1000 1005

Leu Ser Thr Ala Leu Thr Arg Asp Asn Arg His Phe Tyr Asn Gln 1010 1015 1020

<210> 30

<211> 821

<212> PRT

<213> Mus musculus

<400> 30

Met Val Leu Arg Arg Arg Thr Leu His Pro Leu Ser Leu Leu Val Gln 1 5 10 15

Ala Ala Val Leu Ala Glu Thr Leu Ala Leu Gly Thr Leu Pro Ala Phe 20 25 30

Leu Pro Cys Glu Leu Lys Pro His Gly Leu Val Asp Cys Asn Trp Leu 35 40 45

Phe Leu Lys Ser Val Pro Arg Phe Ser Ala Ala Ala Ser Cys Ser Asn 50 55 60

Ile Thr Arg Leu Ser Leu Ile Ser Asn Arg Ile His His Leu His Asn 65 70 75 80

Ser Asp Phe Val His Leu Ser Asn Leu Arg Gln Leu Asn Leu Lys Trp 85 90 95

Asn Cys Pro Pro Thr Gly Leu Ser Pro Leu His Phe Ser Cys His Met 100 105 110

Thr Ile Glu Pro Arg Thr Phe Leu Ala Met Arg Thr Leu Glu Glu Leu 115 120 125

- Asn Leu Ser Tyr Asn Gly Ile Thr Thr Val Pro Arg Leu Pro Ser Ser 130 140
- Asn Ser Leu Ala Gly Leu Tyr Ser Leu Arg Val Leu Phe Met Asp Gly 165 170 175
- Asn Cys Tyr Tyr Lys Asn Pro Cys Thr Gly Ala Val Lys Val Thr Pro 180 185 190
- Gly Ala Leu Leu Gly Leu Ser Asn Leu Thr His Leu Ser Leu Lys Tyr 195 200 205
- Asn Asn Leu Thr Lys Val Pro Arg Gln Leu Pro Pro Ser Leu Glu Tyr 210 215 220
- Leu Leu Val Ser Tyr Asn Leu Ile Val Lys Leu Gly Pro Glu Asp Leu 225 230 235 240
- Ala Asn Leu Thr Ser Leu Arg Val Leu Asp Val Gly Gly Asn Cys Arg 245 250 255
- Arg Cys Asp His Ala Pro Asn Pro Cys Ile Glu Cys Gly Gln Lys Ser 260 265 270
- Leu His Leu His Pro Glu Thr Phe His His Leu Ser His Leu Glu Gly 275 280 285
- Leu Val Leu Lys Asp Ser Ser Leu His Thr Leu Asn Ser Ser Trp Phe 290 295 300
- Gln Gly Leu Val Asn Leu Ser Val Leu Asp Leu Ser Glu Asn Phe Leu 305 310 315 320
- Tyr Glu Ser Ile Asn His Thr Asn Ala Phe Gln Asn Leu Thr Arg Leu 325 330 335
- Arg Lys Leu Asn Leu Ser Phe Asn Tyr Arg Lys Lys Val Ser Phe Ala

340 345 350

Arg Leu His Leu Ala Ser Ser Phe Lys Asn Leu Val Ser Leu Gln Glu 355 360 365

Leu Asn Met Asn Gly Ile Phe Phe Arg Ser Leu Asn Lys Tyr Thr Leu 370 375 380

Arg Trp Leu Ala Asp Leu Pro Lys Leu His Thr Leu His Leu Gln Met 385 390 395 400

Asn Phe Ile Asn Gln Ala Gln Leu Ser Ile Phe Gly Thr Phe Arg Ala 405 410 415

Leu Arg Phe Val Asp Leu Ser Asp Asn Arg Ile Ser Gly Pro Ser Thr 420 425 430

Leu Ser Glu Ala Thr Pro Glu Glu Ala Asp Asp Ala Glu Gln Glu Glu 435

Leu Leu Ser Ala Asp Pro His Pro Ala Pro Leu Ser Thr Pro Ala Ser 450 455 460

Lys Asn Phe Met Asp Arg Cys Lys Asn Phe Lys Phe Thr Met Asp Leu 475 480

Ser Arg Asn Asn Leu Val Thr Ile Lys Pro Glu Met Phe Val Asn Leu 485 490 495

Ser Arg Leu Gln Cys Leu Ser Leu Ser His Asn Ser Ile Ala Gln Ala 500 505 510

Val Asn Gly Ser Gln Phe Leu Pro Leu Thr Asn Leu Gln Val Leu Asp

Leu Ser His Asn Lys Leu Asp Leu Tyr His Trp Lys Ser Phe Ser Glu 530 535 540

Leu Pro Gln Leu Gln Ala Leu Asp Leu Ser Tyr Asn Ser Gln Pro Phe 545 550 560

Ser Met Lys Gly Ile Gly His Asn Phe Ser Phe Val Ala His Leu Ser 565 570 575

Met Leu His Ser Leu Ser Leu Ala His Asn Asp Ile His Thr Arg Val 580 585 590

- Ser Ser His Leu Asn Ser Asn Ser Val Arg Phe Leu Asp Phe Ser Gly 595 600 605
- Asn Gly Met Gly Arg Met Trp Asp Glu Gly Gly Leu Tyr Leu His Phe 610 615 620
- Phe Gln Gly Leu Ser Gly Leu Leu Lys Leu Asp Leu Ser Gln Asn Asn 625 630 635
- Leu His Ile Leu Arg Pro Gln Asn Leu Asp Asn Leu Pro Lys Ser Leu
 . 645 650 655
- Lys Leu Leu Ser Leu Arg Asp Asn Tyr Leu Ser Phe Phe Asn Trp Thr 660 ' 665 670
- Ser Leu Ser Phe Leu Pro Asn Leu Glu Val Leu Asp Leu Ala Gly Asn 675 680 685
- Gln Leu Lys Ala Leu Thr Asn Gly Thr Leu Pro Asn Gly Thr Leu Leu 690 695 700
- Gln Lys Leu Asp Val Ser Ser Asn Ser Ile Val Ser Val Val Pro Ala 705 710 715 720
- Phe Phe Ala Leu Ala Val Glu Leu Lys Glu Val Asn Leu Ser His Asn 725 730 735
- Ile Leu Lys Thr Val Asp Arg Ser Trp Phe Gly Pro Ile Val Met Asn 740 745 750
- Leu Thr Val Leu Asp Val Arg Ser Asn Pro Leu His Cys Ala Cys Gly 755 760 765
- Ala Ala Phe Val Asp Leu Leu Glu Val Gln Thr Lys Val Pro Gly 770 780
- Leu Ala Asn Gly Val Lys Cys Gly Ser Pro Gly Gln Leu Gln Gly Arg
 785 790 795 800
- Ser Ile Phe Ala Gln Asp Leu Arg Leu Cys Leu Asp Glu Val Leu Ser 805 810 815

Trp Asp Cys Phe Gly 820

<210> 31 <211> 3200 <212> DNA <213> Mus musculus

<400> 31

tgtcagaggg agcctcggga gaatcctcca tctcccaaca tggttctccg tcgaaggact 60 ctgcacccct tgtccctcct ggtacaggct gcagtgctgg ctgagactct ggccctgggt 120 accetgeetg cettectace etgtgagetg aageeteatg geetggtgga etgcaattgg 180 ctgttcctga agtctgtacc ccgtttctct gcggcagcat cctgctccaa catcacccgc 240 ctctccttga tctccaaccg tatccaccac ctgcacaact ccgacttcgt ccacctgtcc 300 aacetgegge agetgaacet caagtggaac tgtccaceca etggeettag eeceetgeae 360 ttetettgee acatgaceat tgageeeaga acetteetgg etatgegtae actggaggag 420 ctgaacctga gctataatgg tatcaccact gtgccccgac tgcccagctc cctggtgaat 480 ctgagcctga gccacaccaa catcctggtt ctagatgcta acagcctcgc cggcctatac 540 agcctgcgcg ttctcttcat ggacgggaac tgctactaca agaacccctg cacaggagcg 600 gtgaaggtga ccccaggcgc cctcctgggc ctgagcaatc tcacccatct gtctctgaag 660 tataacaacc tcacaaaggt gccccgccaa ctgcccccca gcctggagta cctcctggtg 720 tcctataacc tcattgtcaa gctggggcct gaagacctgg ccaatctgac ctcccttcga 780 gtacttgatg tgggtgggaa ttgccgtcgc tgcgaccatg cccccaatcc ctgtatagaa 840 tgtggccaaa agtccctcca cctgcaccct gagaccttcc atcacctgag ccatctggaa 900 ggcctggtgc tgaaggacag ctctctccat acactgaact cttcctggtt ccaaggtctg 960 gtcaacctct cggtgctgga cctaagcgag aactttctct atgaaagcat caaccacacc 1020 aatgeettte agaacetaac eegeetgege aageteaace tgteetteaa ttaeegeaag 1080 aaggtateet ttgecegeet ecaectggea agtteettea agaacetggt gteactgeag 1140 gagetgaaca tgaacggcat ettetteege tegetcaaca agtacacget cagatggetg 1200 geogatetge ecaaacteca caetetgeat etteaaatga aetteateaa ecaggeacag 1260 ctcagcatct ttggtacctt ccgagccctt cgctttgtgg acttgtcaga caatcgcatc 1320 agtgggcctt caacgctgtc agaagccacc cctgaagagg cagatgatgc agagcaggag 1380 gagetgttgt etgeggatee teacceaget ecaetgagea eccetgette taagaactte 1440

atggacaggt	gtaagaactt	caagttcacc	atggacctgt	ctcggaacaa	cctggtgact	1500
atcaagccag	agatgtttgt	caatctctca	cgcctccagt	gtcttagcct	gagccacaac	1560
tccattgcac	aggctgtcaa	tggctctcag	ttcctgccgc	tgactaatct	gcaggtgctg	1620
gacctgtccc	ataacaaact	ggacttgtac	cactggaaat	cgttcagtga	gctaccacag	1680
ttgcaggccc	tggacctgag	ctacaacagc	cagcccttta	gcatgaaggg	tataggccac	1740
aatttcagtt	ttgtggccca	tctgtccatg	ctacacagcc	ttagcctggc	acacaatgac	1800
attcataccc	gtgtgtcctc	acatctcaac	agcaactcag	tgaggtttct	tgacttcagc	1860
ggcaacggta	tgggccgcat	gtgggatgag	gggggccttt	atctccattt	cttccaaggc	1920
ctgagtggcc	tgctgaagct	ggacctgtct	caaaataacc	tgcatatcct	ccggccccag	1980
aaccttgaca	acctccccaa	gagcctgaag	ctgctgagcc	tccgagacaa	ctacctatct	2040
ttctttaact	ggaccagtct	gtccttcctg	cccaacctgg	aagtcctaga	cctggcaggc	2100
aaccagctaa	aggccctgac	caatggcacc	ctgcctaatg	gcaccctcct	ccagaaactg	2160
gatgtcagca	gcaacagtat	cgtctctgtg	gtcccagcct	tettegetet	ggcggtcgag	2220
ctgaaagagg	tcaacctcag	ccacaacatt	ctcaagacgg	tggatcgctc	ctggtttggg	2280
cccattgtga	tgaacctgac	agttctagac	gtgagaagca	accetetgea	ctgtgcctgt	2340
ggggcagcct	tcgtagactt	actgttggag	gtgcagacca	aggtgcctgg	cctggctaat	2400
ggtgtgaagt	gtggcagccc	cggccagctg	cagggccgta	gcatcttcgc	acaggacctg	2460
cggctgtgcc	tggatgaggt	cctctcttgg	gactgctttg	gcctttcact	cttggctgtg	2520
gccgtgggca	tggtggtgcc	tatactgcac	catctctgcg	gctgggacgt	ctggtactgt	2580
tttcatctgt	gcctggcatg	gctacctttg	ctggcccgca	gccgacgcag	cgcccaagct	2640
ctcccctatg	atgccttcgt	ggtgttcgat	aaggcacaga	gcgcagttgc	ggactgggtg	2700
tataacgagc	tgcgggtgcg	gctggaggag	cggcgcggtc	gccgagccct	acgcttgtgt	2760
ctggaggacc	gagattggct	gcctggccag	acgctcttcg	agaacctctg	ggcttccatc	2820
tatgggagcc	gcaagactct	atttgtgctg	gcccacacgg	accgcgtcag	tggcctcctg	2880
cgcaccagct	tectgetgge	tcagcagcgc	ctgttggaag	accgcaagga	cgtggtggtg	2940
ttggtgatcc	tgcgtccgga	tgcccaccgc	tcccgctatg	tgcgactgcg	ccagcgtctc	3000
tgccgccaga	gtgtgctctt	ctggccccag	cagcccaacg	ggcagggggg	cttctgggcc	3060
cagctgagta	cagccctgac	tagggacaac	cgccacttct	ataaccagaa	cttctgccgg	3120
ggacctacag	cagaatagct	cagagcaaca	gctggaaaca	gctgcatctt	catgcctggt	3180
tcccgagttg	ctctgcctgc					3200

÷: .

<210> 32 <211> 2463 <212> DNA <213> Mus musculus

<400> 32

atggttetee gtegaaggae tetgeaceee ttgteeetee tggtacagge tgeagtgetg 60 gctgagactc tggccctggg taccctgcct gccttcctac cctgtgagct gaagcctcat 120 ggcctggtgg actgcaattg gctgttcctg aagtctgtac cccgtttctc tgcggcagca 180 tectgeteca acateacceg cetetecttg atetecaace gtatecacca cetgeacaac 240 tecgaetteg tecacetgte caacetgegg cagetgaace teaagtggaa etgtecacee 300 actggcctta gccccctgca cttctcttgc cacatgacca ttgagcccag aaccttcctg 360 gctatgcgta cactggagga gctgaacctg agctataatg gtatcaccac tgtgccccga 420 ctgcccagct ccctggtgaa tctgagcctg agccacacca acatcctggt tctagatgct 480 aacageeteg eeggeetata eageetgege gttetettea tggaegggaa etgetaetae 540 aagaacccct gcacaggagc ggtgaaggtg accccaggcg ccctcctggg cctgagcaat 600 ctcacccatc tgtctctgaa gtataacaac ctcacaaagg tgccccgcca actgccccc 660 agcctggagt acctcctggt gtcctataac ctcattgtca agctggggcc tgaagacctg 720 gccaatctga cetecetteg agtacttgat gtgggtggga attgccgtcg ctgcgaccat 780 gececeaate cetgtataga atgtggeeaa aagteeetee acetgeacee tgagacette 840 catcacctga gccatctgga aggcctggtg ctgaaggaca gctctctcca tacactgaac 900 tetteetggt tecaaggtet ggteaacete teggtgetgg acetaagega gaactttete 960 tatgaaagca tcaaccacac caatgccttt cagaacctaa cccgcctgcg caagctcaac 1020 etgteettea attacegeaa gaaggtatee tttgeeegee teeacetgge aagtteette 1080 aagaacctgg tgtcactgca ggagctgaac atgaacggca tcttcttccg ctcgctcaac 1140 aagtacacgc tcagatggct ggccgatctg cccaaactcc acactctgca tcttcaaatg 1200 aacttcatca accaggcaca gctcagcatc tttggtacct tccgagccct tcgctttgtg 1260 gacttgtcag acaatcgcat cagtgggcct tcaacgctgt cagaagccac ccctgaagag 1320 gcagatgatg cagagcagga ggagctgttg tctgcggatc ctcacccagc tccactgagc 1380 acccctgctt ctaagaactt catggacagg tgtaagaact tcaagttcac catggacctg 1440 teteggaaca acctggtgac tatcaageca gagatgtttg teaatetete acgeetecag 1500 tgtcttagcc tgagccacaa ctccattgca caggctgtca atggctctca gttcctgccg 1560

ctgactaatc tgcaggtgct ggacctgtcc cataacaaac tggacttgta ccactggaaa 1620 tegtteagtg agetaceaea gttgeaggee ctggacetga getacaaeag ceagecettt 1680 agcatgaagg gtataggcca caatttcagt tttgtggccc atctgtccat gctacacagc 1740 cttagcctgg cacacaatga cattcatacc cqtgtgtcct cacatctcaa cagcaactca 1800 gtgaggtttc ttgacttcag cggcaacggt atgggccgca tgtgggatga ggggggcctt 1860 tatctccatt tcttccaagg cctgagtggc ctgctgaagc tggacctgtc tcaaaataac 1920 ctgcatatcc tccggcccca gaaccttgac aacctcccca agagcctgaa gctgctgagc 1980 ctccgagaca actacctatc tttctttaac tggaccagtc tgtccttcct gcccaacctg 2040 gaagteetag acetggeagg caaceageta aaggeeetga eeaatggeae eetgeetaat 2100 ggcaccctcc tccagaaact ggatgtcagc agcaacagta tcgtctctgt ggtcccagcc 2160 ttettegete tggeggtega getgaaagag gteaacetea gecacaacat teteaagaeg 2220 gtggatcgct cctggtttgg gcccattgtg atgaacctga cagttctaga cgtgagaagc 2280 aaccetetge actgtgeetg tggggeagee ttegtagaet tactgttgga ggtgeagaee 2340 aaggtgcctg gcctggctaa tggtgtgaag tgtggcagcc ccggccagct gcagggccgt 2400 agcatcttcg cacaggacct gcggctgtgc ctggatgagg tcctctcttg ggactgcttt 2460 ggc 2463

. . d

<210> 33

<211> 1032

<212> PRT

<213> Homo sapiens

<400> 33

Met Gly Phe Cys Arg Ser Ala Leu His Pro Leu Ser Leu Leu Val Gln
1 5 10 15

Ala Ile Met Leu Ala Met Thr Leu Ala Leu Gly Thr Leu Pro Ala Phe 20 25 30

Leu Pro Cys Glu Leu Gln Pro His Gly Leu Val Asn Cys Asn Trp Leu 35 40 45

Phe Leu Lys Ser Val Pro His Phe Ser Met Ala Ala Pro Arg Gly Asn 50 55 60

والمراجع والمنتقل والمراجع وال

Val Thr Ser Leu Ser Leu Ser Ser Asn Arg Ile His His Leu His Asp 65 70 75 80

Ser Asp Phe Ala His Leu Pro Ser Leu Arg His Leu Asn Leu Lys Trp 85 90 95

- Asn Cys Pro Pro Val Gly Leu Ser Pro Met His Phe Pro Cys His Met 100 105 110
- Thr Ile Glu Pro Ser Thr Phe Leu Ala Val Pro Thr Leu Glu Glu Leu 115 120 125
- Asn Leu Ser Tyr Asn Asn Ile Met Thr Val Pro Ala Leu Pro Lys Ser 130 135 140
- Leu Ile Ser Leu Ser Leu Ser His Thr Asn Ile Leu Met Leu Asp Ser 145 150 155 160
- Ala Ser Leu Ala Gly Leu His Ala Leu Arg Phe Leu Phe Met Asp Gly 165 170 175
- Asn Cys Tyr Tyr Lys Asn Pro Cys Arg Gln Ala Leu Glu Val Ala Pro 180 185 190
- Gly Ala Leu Leu Gly Leu Gly Asn Leu Thr His Leu Ser Leu Lys Tyr 195 200 205
- Asn Asn Leu Thr Val Val Pro Arg Asn Leu Pro Ser Ser Leu Glu Tyr 210 220
- Leu Leu Leu Ser Tyr Asn Arg Ile Val Lys Leu Ala Pro Glu Asp Leu 225 230 235 240
- Ala Asn Leu Thr Ala Leu Arg Val Leu Asp Val Gly Gly Asn Cys Arg 245 250 255
- Arg Cys Asp His Ala Pro Asn Pro Cys Met Glu Cys Pro Arg His Phe 260 265 270
- Pro Gln Leu His Pro Asp Thr Phe Ser His Leu Ser Arg Leu Glu Gly 275 280 285
- Leu Val Leu Lys Asp Ser Ser Leu Ser Trp Leu Asn Ala Ser Trp Phe 290 295 300
- Arg Gly Leu Gly Asn Leu Arg Val Leu Asp Leu Ser Glu Asn Phe Leu

305 310 315 320

Tyr Lys Cys Ile Thr Lys Thr Lys Ala Phe Gln Gly Leu Thr Gln Leu 325 330 335

Arg Lys Leu Asn Leu Ser Phe Asn Tyr Gln Lys Arg Val Ser Phe Ala 340 345 350

His Leu Ser Leu Ala Pro Ser Phe Gly Ser Leu Val Ala Leu Lys Glu 355 360 365

Leu Asp Met His Gly Ile Phe Phe Arg Ser Leu Asp Glu Thr Thr Leu 370 375 380

Arg Pro Leu Ala Arg Leu Pro Met Leu Gln Thr Leu Arg Leu Gln Met 385 390 395 400

Asn Phe Ile Asn Gln Ala Gln Leu Gly Ile Phe Arg Ala Phe Pro Gly 405 410 415

Leu Arg Tyr Val Asp Leu Ser Asp Asn Arg Ile Ser Gly Ala Ser Glu 420 425 430 .

Leu Thr Ala Thr Met Gly Glu Ala Asp Gly Gly Glu Lys Val Trp Leu
435 440 445

Gln Pro Gly Asp Leu Ala Pro Ala Pro Val Asp Thr Pro Ser Ser Glu 450 455 460

Asp Phe Arg Pro Asn Cys Ser Thr Leu Asn Phe Thr Leu Asp Leu Ser 465 470 475 480

Arg Asn Asn Leu Val Thr Val Gln Pro Glu Met Phe Ala Gln Leu Ser 485 490 495

His Leu Gln Cys Leu Arg Leu Ser His Asn Cys Ile Ser Gln Ala Val 500 505 510

Asn Gly Ser Gln Phe Leu Pro Leu Thr Gly Leu Gln Val Leu Asp Leu 515 520 525

Ser Arg Asn Lys Leu Asp Leu Tyr His Glu His Ser Phe Thr Glu Leu 530 535 540

Pro Arg Leu Glu Ala Leu Asp Leu Ser Tyr Asn Ser Gln Pro Phe Gly 555 550

- Met Gln Gly Val Gly His Asn Phe Ser Phe Val Ala His Leu Arg Thr 565 570 575
- Leu Arg His Leu Ser Leu Ala His Asn Asn Ile His Ser Gln Val Ser 580 585 590
- Gln Gln Leu Cys Ser Thr Ser Leu Arg Ala Leu Asp Phe Ser Gly Asn 595 600 605
- Ala Leu Gly His Met Trp Ala Glu Gly Asp Leu Tyr Leu His Phe Phe 610 620
- Gln Gly Leu Ser Gly Leu Ile Trp Leu Asp Leu Ser Gln Asn Arg Leu 625 630 635 640
- His Thr Leu Leu Pro Gln Thr Leu Arg Asn Leu Pro Lys Ser Leu Gln 645 655
- Val Leu Arg Leu Arg Asp Asn Tyr Leu Ala Phe Phe Lys Trp Trp Ser 660 665 670
- Leu His Phe Leu Pro Lys Leu Glu Val Leu Asp Leu Ala Gly Asn Arg 675 680 685
- Leu Lys Ala Leu Thr Asn Gly Ser Leu Pro Ala Gly Thr Arg Leu Arg 690 695 700
- Arg Leu Asp Val Ser Cys Asn Ser Ile Ser Phe Val Ala Pro Gly Phe 705 710 715 720
- Phe Ser Lys Ala Lys Glu Leu Arg Glu Leu Asn Leu Ser Ala Asn Ala 725 730 735
- Leu Lys Thr Val Asp His Ser Trp Phe Gly Pro Leu Ala Ser Ala Leu 740 745 750
- Gln Ile Leu Asp Val Ser Ala Asn Pro Leu His Cys Ala Cys Gly Ala 755 760 765
- Ala Phe Met Asp Phe Leu Leu Glu Val Gln Ala Ala Val Pro Gly Leu 770 780

Pro Ser Arg Val Lys Cys Gly Ser Pro Gly Gln Leu Gln Gly Leu Ser 785 790 795 800

- Ile Phe Ala Gln Asp Leu Arg Leu Cys Leu Asp Glu Ala Leu Ser Trp 805 810 815
- Asp Cys Phe Ala Leu Ser Leu Leu Ala Val Ala Leu Gly Leu Gly Val 820 825 830
- Pro Met Leu His His Leu Cys Gly Trp Asp Leu Trp Tyr Cys Phe His 835 840 845
- Leu Cys Leu Ala Trp Leu Pro Trp Arg Gly Arg Gln Ser Gly Arg Asp 850 855 860
- Glu Asp Ala Leu Pro Tyr Asp Ala Phe Val Val Phe Asp Lys Thr Gln 865 870 875 880
- Ser Ala Val Ala Asp Trp Val Tyr Asn Glu Leu Arg Gly Gln Leu Glu 885 890 895
- Glu Cys Arg Gly Arg Trp Ala Leu Arg Leu Cys Leu Glu Glu Arg Asp 900 905 910
- Trp Leu Pro Gly Lys Thr Leu Phe Glu Asn Leu Trp Ala Ser Val Tyr 915 920 925
- Gly Ser Arg Lys Thr Leu Phe Val Leu Ala His Thr Asp Arg Val Ser 930 935 940
- Gly Leu Leu Arg Ala Ser Phe Leu Leu Ala Gln Gln Arg Leu Leu Glu 945 950 955 960
- Asp Arg Lys Asp Val Val Val Leu Val Ile Leu Ser Pro Asp Gly Arg 965 970 975
- Arg Ser Arg Tyr Val Arg Leu Arg Gln Arg Leu Cys Arg Gln Ser Val 980 985 990
- Leu Leu Trp Pro His Gln Pro Ser Gly Gln Arg Ser Phe Trp Ala Gln 995 1000 1005
- Leu Gly Met Ala Leu Thr Arg Asp Asn His His Phe Tyr Asn Arg 1010 1015 1020

Asn Phe Cys Gln Gly Pro Thr Ala Glu 1025 1030

<210> 34

<211> 820

<212> PRT

<213> Homo sapiens

<400> 34

Met Gly Phe Cys Arg Ser Ala Leu His Pro Leu Ser Leu Leu Val Gln 1 5 10 15

Ala Ile Met Leu Ala Met Thr Leu Ala Leu Gly Thr Leu Pro Ala Phe 20 25 30

Leu Pro Cys Glu Leu Gln Pro His Gly Leu Val Asn Cys Asn Trp Leu 35 40 45

Phe Leu Lys Ser Val Pro His Phe Ser Met Ala Ala Pro Arg Gly Asn 50 55 60

Val Thr Ser Leu Ser Leu Ser Ser Asn Arg Ile His His Leu His Asp 65 70 75 80

Ser Asp Phe Ala His Leu Pro Ser Leu Arg His Leu Asn Leu Lys Trp 85 90 95

Asn Cys Pro Pro Val Gly Leu Ser Pro Met His Phe Pro Cys His Met 100 105 110

Thr Ile Glu Pro Ser Thr Phe Leu Ala Val Pro Thr Leu Glu Glu Leu 115 120 125

Asn Leu Ser Tyr Asn Asn Ile Met Thr Val Pro Ala Leu Pro Lys Ser 130 140

Leu Ile Ser Leu Ser Leu Ser His Thr Asn Ile Leu Met Leu Asp Ser 155 160

Ala Ser Leu Ala Gly Leu His Ala Leu Arg Phe Leu Phe Met Asp Gly 165 170 175

Asn Cys Tyr Tyr Lys Asn Pro Cys Arg Gln Ala Leu Glu Val Ala Pro 180 185 190

Gly Ala Leu Leu Gly Leu Gly Asn Leu Thr His Leu Ser Leu Lys Tyr 195 200 205

- Asn Asn Leu Thr Val Val Pro Arg Asn Leu Pro Ser Ser Leu Glu Tyr 210 215 220
- Leu Leu Ser Tyr Asn Arg Ile Val Lys Leu Ala Pro Glu Asp Leu 225 230 235 240
- Ala Asn Leu Thr Ala Leu Arg Val Leu Asp Val Gly Gly Asn Cys Arg 245 250 255
- Arg Cys Asp His Ala Pro Asn Pro Cys Met Glu Cys Pro Arg His Phe 260 265 270
- Pro Gln Leu His Pro Asp Thr Phe Ser His Leu Ser Arg Leu Glu Gly 275 280 285
- Leu Val Leu Lys Asp Ser Ser Leu Ser Trp Leu Asn Ala Ser Trp Phe 290 295 300
- Arg Gly Leu Gly Asn Leu Arg Val Leu Asp Leu Ser Glu Asn Phe Leu 305 310 315 320
- Tyr Lys Cys Ile Thr Lys Thr Lys Ala Phe Gln Gly Leu Thr Gln Leu 325 330 335
- Arg Lys Leu Asn Leu Ser Phe Asn Tyr Gln Lys Arg Val Ser Phe Ala 340 345 350
- His Leu Ser Leu Ala Pro Ser Phe Gly Ser Leu Val Ala Leu Lys Glu 355 360 365
- Leu Asp Met His Gly Ile Phe Phe Arg Ser Leu Asp Glu Thr Thr Leu 370 380
- Arg Pro Leu Ala Arg Leu Pro Met Leu Gln Thr Leu Arg Leu Gln Met 385 390 395 400
- Asn Phe Ile Asn Gln Ala Gln Leu Gly Ile Phe Arg Ala Phe Pro Gly
 405 410 415
- Leu Arg Tyr Val Asp Leu Ser Asp Asn Arg Ile Ser Gly Ala Ser Glu

420

425

430

Leu Thr Ala Thr Met Gly Glu Ala Asp Gly Gly Glu Lys Val Trp Leu 435 440 445

Gln Pro Gly Asp Leu Ala Pro Ala Pro Val Asp Thr Pro Ser Ser Glu 450 455 460

Asp Phe Arg Pro Asn Cys Ser Thr Leu Asn Phe Thr Leu Asp Leu Ser 465 470 475 480

Arg Asn Asn Leu Val Thr Val Gln Pro Glu Met Phe Ala Gln Leu Ser 485 490 495

His Leu Gln Cys Leu Arg Leu Ser His Asn Cys Ile Ser Gln Ala Val 500 505 510

Asn Gly Ser Gln Phe Leu Pro Leu Thr Gly Leu Gln Val Leu Asp Leu 515 520 525

Ser Arg Asn Lys Leu Asp Leu Tyr His Glu His Ser Phe Thr Glu Leu 530 540

Pro Arg Leu Glu Ala Leu Asp Leu Ser Tyr Asn Ser Gln Pro Phe Gly 545 550 555 560

Met Gln Gly Val Gly His Asn Phe Ser Phe Val Ala His Leu Arg Thr 565 570 575

Leu Arg His Leu Ser Leu Ala His Asn Asn Ile His Ser Gln Val Ser 580 585 590

Gln Gln Leu Cys Ser Thr Ser Leu Arg Ala Leu Asp Phe Ser Gly Asn 595 600 605

Ala Leu Gly His Met Trp Ala Glu Gly Asp Leu Tyr Leu His Phe Phe 610 620

Gln Gly Leu Ser Gly Leu Ile Trp Leu Asp Leu Ser Gln Asn Arg Leu 625 630 635 640

His Thr Leu Leu Pro Gln Thr Leu Arg Asn Leu Pro Lys Ser Leu Gln 645 650 655

Val Leu Arg Leu Arg Asp Asn Tyr Leu Ala Phe Phe Lys Trp Trp Ser 660 665 670

Leu His Phe Leu Pro Lys Leu Glu Val Leu Asp Leu Ala Gly Asn Arg 675 680 685

Leu Lys Ala Leu Thr Asn Gly Ser Leu Pro Ala Gly Thr Arg Leu Arg 690 695 700

Arg Leu Asp Val Ser Cys Asn Ser Ile Ser Phe Val Ala Pro Gly Phe 705 710 715 720

Phe Ser Lys Ala Lys Glu Leu Arg Glu Leu Asn Leu Ser Ala Asn Ala 725 730 . 735

Leu Lys Thr Val Asp His Ser Trp Phe Gly Pro Leu Ala Ser Ala Leu 740 745 750

Gln Ile Leu Asp Val Ser Ala Asn Pro Leu His Cys Ala Cys Gly Ala
755 760 765

Ala Phe Met Asp Phe Leu Leu Glu Val Gln Ala Ala Val Pro Gly Leu 770 775 780

Pro Ser Arg Val Lys Cys Gly Ser Pro Gly Gln Leu Gln Gly Leu Ser 785 790 795 800

Ile Phe Ala Gln Asp Leu Arg Leu Cys Leu Asp Glu Ala Leu Ser Trp 805 810 815

Asp Cys Phe Ala 820

<210> 35

<211> 3352

<212> DNA

<213> Homo sapiens

<400> 35

aggetggtat aaaaatetta etteetetat tetetgagee getgetgeee etgtgggaag 60 ggacetegag tgtgaageat eetteeetgt agetgetgte eagtetgeee gecagaeeet 120 etggagaage eeetgeeee eageatgggt ttetgeegea gegeeetgea eeegetgtet 180 eteetggtge aggeeateat getggeeatg accetggeee tgggtaeett geetgeette 240 etaceetgtg ageteeagee eeaeggeetg gtgaaetgea actggetgtt eetgaagtet 300

gtgccccact tctccatggc	agcaccccgt	ggcaatgtca	ccagcctttc	cttgtcctcc	360
aaccgcatcc accacctcca	tgattctgac	tttgcccacc	tgcccagcct	gcggcatctc	420
aacctcaagt ggaactgccc	gccggttggc	ctcagcccca	tgcacttccc	ctgccacatg	480
accatcgagc ccagcacctt	cttggctgtg	cccaccctgg	aagagctaaa	cctgagctac	540
aacaacatca tgactgtgcc	tgcgctgccc	aaatccctca	tatccctgtc	cctcagccat	600
accaacatcc tgatgctaga	ctctgccagc	ctcgccggcc	tgcatgccct	gcgcttccta	660
ttcatggacg gcaactgtta	ttacaagaac	ccctgcaggc	aggcactgga	ggtggccccg	720
ggtgccctcc ttggcctggg	caacctcacc	cacctgtcac	tcaagtacaa	caacctcact	780
gtggtgcccc gcaacctgcc	ttccagcctg	gagtatctgc	tgttgtccta	caaccgcatc	840
gtcaaactgg cgcctgagga	cctggccaat	ctgaccgccc	tgcgtgtgct	cgatgtgggc	900
ggaaattgcc gccgctgcga	ccacgetecc	aacccctgca	tggagtgccc	tcgtcacttc	960
ccccagctac atcccgatac	cttcagccac	ctgagccgtc	ttgaaggcct	ggtgttgaag	1020
gacagttctc tctcctggct	gaatgccagt	tggttccgtg	ggctgggaaa	cctccgagtg	1080
ctggacctga gtgagaactt	cctctacaaa	tgcatcacta	aaaccaaggc	cttccagggc	1140
ctaacacagc tgcgcaagct	taacctgtcc	ttcaattacc	aaaagagggt	gtcctttgcc	1200
cacctgtctc tggccccttc	cttcgggagc	ctggtcgccc	tgaaggagct	ggacatgcac	1260
ggcatcttct tccgctcact	cgatgagacc	acgeteegge	cactggcccg	cctgcccatg	1320
ctccagactc tgcgtctgca	gatgaacttc	atcaaccagg	cccagctcgg	catcttcagg	1380
gccttccctg gcctgcgcta	cgtggacctg	tcggacaacc	gcatcagcgg	agcttcggag	1440
ctgacagcca ccatggggga	ggcagatgga	ggggagaagg	tctggctgca	gcctggggac	1500
cttgctccgg ccccagtgga	cactcccagc	tctgaagact	tcaggcccaa	ctgcagcacc	1560
ctcaacttca ccttggatct	gtcacggaac	aacctggtga	ccgtgcagcc	ggagatgttt	1620
gcccagctct cgcacctgca	gtgcctgcgc	ctgagccaca	actgcatctc	gcaggcagtc	1680
aatggctccc agttcctgcc	gctgaccggt	ctgcaggtgc	tagacctgtc	ccgcaataag	1740
ctggacctct accacgagca	ctcattcacg	gagctaccgc	gactggaggc	cctggacctc	1800
agctacaaca gccagccctt	tggcatgcag	ggcgtgggcc	acaacttcag	cttcgtggct	1860
cacctgcgca ccctgcgcca	cctcagcctg	gcccacaaca	acatccacag	ccaagtgtcc	1920
cagcagetet geagtacgte	gctgcgggcc	ctggacttca	gcggcaatgc	actgggccat	1980
atgtgggccg agggagacct	ctatctgcac	ttcttccaag	gcctgagcgg	tttgatctgg	2040

ctggacttgt	cccagaaccg	cctgcacacc	ctcctgcccc	aaaccctgcg	caacctcccc	2100
aagagcctac	aggtgctgcg	tctccgtgac	aattacctgg	ccttctttaa	gtggtggagc	2160
ctccacttcc	tgcccaaact	ggaagtcctc	gacctggcag	gaaaccggct	gaaggccctg	2220
accaatggca	gcctgcctgc	tggcacccgg	ctccggaggc	tggatgtcag	ctgcaacagc	2280
atcagcttcg	tggccccgg	cttcttttcc	aaggccaagg	agctgcgaga	gctcaacctt	2340
agcgccaacg	ccctcaagac	agtggaccac	tcctggtttg	ggcccctggc	gagtgccctg	2400
caaatactag	atgtaagcgc	caaccctctg	cactgcgcct	gtggggcggc	ctttatggac	2460
ttcctgctgg	aggtgcaggc	tgccgtgccc	ggtctgccca	gccgggtgaa	gtgtggcagt	2520
ccgggccagc	tccagggcct	cagcatcttt	gcacaggacc	tgcgcctctg	cctggatgag	2580
gccctctcct	gggactgttt	egeceteteg	ctgctggctg	tggctctggg	cctgggtgtg	2640
cccatgctgc	atcacctctg	tggctgggac	ctctggtact	gcttccacct	gtgcctggcc	2700
tggcttccct	ggcgggggcg	gcaaagtggg	cgagatgagg	atgccctgcc	ctacgatgcc	2760
ttcgtggtct	tcgacaaaac	gcagagcgca	gtggcagact	gggtgtacaa	cgagcttcgg	2820
gggcagctgg	aggagtgccg	tgggcgctgg	gcactccgcc	tgtgcctgga	ggaacgcgac	2880
tggctgcctg	gcaaaaccct	ctttgagaac	ctgtgggcct	cggtctatgg	cagccgcaag	2940
acgctgtttg	tgctggccca	cacggaccgg	gtcagtggtc	tcttgcgcgc	cagcttcctg	3000
ctggcccagc	agcgcctgct	ggaggaccgc	aaggacgtcg	tggtgctggt	gatcctgagc	3060
cctgacggcc	gccgctcccg	ctacgtgcgg	ctgcgccagc	gcctctgccg	ccagagtgtc	3120
ctcctctggc	cccaccagcc	cagtggtcag	cgcagcttct	gggcccagct	gggcatggcc	3180
ctgaccaggg	acaaccacca	cttctataac	cggaacttct	gccagggacc	cacggccgaa	3240
tagccgtgag	ccggaatcct	gcacggtgcc	acctccacac	tcacctcacc	tatgaatgaa	3300
tggtctgacc	ctcccctgct	cgcctccctc	accccacacc	tgacacagag	ca	3352
210. 26						

<210> 36

<211> 2460

<212> DNA

<213> Homo sapiens

<400> 36

atgggtttet geegeagege cetgeaceeg etgtetetee tggtgeagge cateatgetg 60 geeatgacee tggceetggg tacettgeet geetteetae eetgtgaget eeageeceae 120 ggcetggtga actgeaactg getgtteetg aagtetgtge eecacttete catggeagea 180 eecegtggea atgteaceag cettteettg teetecaace geatecacea eetecatgat 240

tctgactttg	cccacctgcc	cagcctgcgg	catctcaacc	tcaagtggaa	ctgcccgccg	300
gttggcctca	gccccatgca	cttcccctgc	cacatgacca	tegageceag	caccttcttg	360
gctgtgccca	ccctggaaga	gctaaacctg	agctacaaca	acatcatgac	tgtgcctgcg	420
ctgcccaaat	ccctcatatc	cctgtccctc	agccatacca	acatcctgat	gctagactct	480
gccagcctcg	ccggcctgca	tgccctgcgc	ttcctattca	tggacggcaa	ctgttattac	540
aagaacccct	gcaggcaggc	actggaggtg	gccccgggtg	ccctccttgg	cctgggcaac	600
ctcacccacc	tgtcactcaa	gtacaacaac	ctcactgtgg	tgccccgcaa	cctgccttcc	- 660
agcctggagt	atctgctgtt	gtcctacaac	cgcatcgtca	aactggcgcc	tgaggacctg	720
gccaatctga	ccgccctgcg	tgtgctcgat	gtgggcggaa	attgccgccg	ctgcgaccac	780
gctcccaacc	cctgcatgga	gtgccctcgt	cacttccccc	agctacatcc	cgataccttc	840
agccacctga	gccgtcttga	aggcctggtg	ttgaaggaca	gttctctctc	ctggctgaat	900
gccagttggt	tccgtgggct	gggaaacctc	cgagtgctgg	acctgagtga	gaacttcctc	960
tacaaatgca	tcactaaaac	caaggccttc	cagggcctaa	cacagetgeg	caagcttaac	1020
ctgtccttca	attaccaaaa	gagggtgtcc	tttgcccacc	tgtctctggc	cccttccttc	1080
gggagcctgg	tcgccctgaa	ggagctggac	atgcacggca	tattattaag	ctcactcgat	1140
gagaccacgc	tccggccact	ggcccgcctg	cccatgctcc	agactctgcg	tctgcagatg	1200
aacttcatca	accaggccca	gctcggcatc	ttcagggcct	tecctggeet	gcgctacgtg	1260
gacctgtcgg	acaaccgcat	cagcggagct	tcggagctga	cagccaccat	gggggaggca	1320
gatggagggg	agaaggtctg	gctgcagcct	ggggaccttg	ctccggcccc	agtggacact	1380
cccagctctg	aagacttcag	gcccaactgc	agcaccctca	acttcacctt	ggatctgtca	1440
cggaacaacc	tggtgaccgt	gcagccggag	atgtttgccc	agctctcgca	cctgcagtgc	1500
ctgcgcctga	gccacaactg	catctcgcag	gcagtcaatg	gctcccagtt	cctgccgctg	1560
accggtctgc	aggtgctaga	cctgtcccgc	aataagctgg	acctctacca	cgagcactca	1620
ttcacggagc	taccgcgact	ggaggccctg	gacctcagct	acaacagcca	gccctttggc	1680
atgcagggcg	tgggccacaa	cttcagcttc	gtggctcacc	tgcgcaccct	gcgccacctc	1740
agcctggccc	acaacaacat	ccacagccaa	gtgtcccagc	agctctgcag	tacgtcgctg	1800
cgggccctgg	acttcagcgg	caatgcactg	ggccatatgt	gggccgaggg	agacctctat	1860
ctgcacttct	tecaaggeet	gagcggtttg	atctggctgg	acttgtccca	gaaccgcctg	1920
cacaccctcc	tgccccaaac	cctgcgcaac	ctccccaaga	gcctacaggt	gctgcgtctc	1980
cgtgacaatt	acctggcctt	ctttaagtgg	tggagcctcc	acttcctgcc	caaactggaa	2040

gtcctcg	acc tggcaggaaa	ccggctgaag	gccctgacca	atggcagcct	geetgetgge	2100
acccggc	tcc ggaggctgga	tgtcagctgc	aacagcatca	gcttcgtggc	ccccggcttc	2160
ttttcca	agg ccaaggagct	gcgagagctc	aaccttagcg	ccaacgccct	caagacagtg	2220
gaccact	cct ggtttgggcc	cctggcgagt	gccctgcaaa	tactagatgt	aagcgccaac	2280
cctctgo	act gcgcctgtgg	ggcggccttt	atggacttcc	tgctggaggt	gcaggctgcc	2340
gtgcccg	gtc tgcccagccg	ggtgaagtgt	ggcagtccgg	gccagctcca	gggcctcagc	2400
atctttg	cac aggacctgcg	cctctgcctg	gatgaggccc	tctcctggga	ctgtttcgcc	2460
	37 26 DNA Artificial seq	uence				
<220> <223>	Synthetic olig	onucleotide				
<400> accttgo	37 ectg cettectace	ctgtga				26
<210><211><211><212>	38 21 DNA Artificial seq	uence			-	
<220> <223>	Synthetic olig					
<400>	38					
gtccgtg	gtgg gccagcacaa	a				21
<210>	39 20					
<212>	DNA					
<213>	Artificial seg	uence				
<220>						
<223>	Synthetic olig	ponucleotide				
<400>	39					
tccatg	acgt ttttgatgtt					20
<210>	40					
<211>	20					
<212>						
<213>	Artificial seg	quence				
<220>						
<223>	Synthetic olig	onucleotide	ł			

<400> tccata	40 Bacgt ttttgatgtt	20
		20
<210>	41	
<211>	20	
<212>	DNA	
	Artificial sequence	
	•	
<220>		
<223>	Synthetic oligonucleotide	
<400>		
tccato	cacgt ttttgatgtt	20
<210>	40	
<211>		
<212>		
<213>	Artificial sequence	
<220>		
	Synthetic oligonucleotide	
12237	Synthetic Oligonucleotide	
<400>	42	
	acgt ttttgatgtt	
		20
<210>	43	
<211>	20	
<212>	DNA	
	Artificial sequence	
<220>		
<223>	Synthetic oligonucleotide	
<400>	43	
tccatg	gcgt ttttgatgtt	20
		_ •
-2110 :	**	
<210>		
<211>		
<212>	_	
<213>	Artificial sequence	
<220>		
	Combbatta 23 23	
<223>	Synthetic oligonucleotide	
<400>	44	
	ccgt ttttgatgtt	
cccacg		20
<210>	45	
<211>		
	DNA	
<213>		
~4137	Artificial sequence	
<220>		

WO 2	004/026888	PCT/US2003/029577
<223>	Synthetic oligonucleotide	
<400>		
cccatg	tcgt ttttgatgtt	20
<210>	46	
<211>		
<212>		
<213>	Artificial sequence	
<220>		
<223>	Synthetic oligonucleotide	
<400>	46	
tccatg	atgt ttttgatgtt	20
<210>	47	•
<211>		
<212>		
<213>	Artificial sequence	
<220>		
<223>	Synthetic oligonucleotide	
<400>	47	
tccatg	aagt ttttgatgtt	20
<210>	48	
<211>		
<212>		
<213>	Artificial sequence	
<220>		
<223>	Synthetic oligonucleotide	
<400>	48	•
tccatg	aggt ttttgatgtt	20
<210>	49	
<211>		
<212>		
<213>	Artificial sequence	
<220>		
<223>	Synthetic oligonucleotide	
<400>	49	
tccatg	acat ttttgatgtt	20
<210>	50	
<211>		
<212>	Artificial sequence	

<220> <223>	Synthetic oligonucleotide	
<400> tccatga	50 acct ttttgatgtt	20
<210>		
<211> <212>		
	Artificial sequence	
<220>		
<223>	Synthetic oligonucleotide	
<400>	51	
tccatg	actt ttttgatgtt	20
<210>	52	
<211>		
<212>	Artificial sequence	
72137	ALCITICIAL SEQUENCE	
<220>		
<223>	Synthetic oligonucleotide	
<400>	52	
tccatg	acgc ttttgatgtt	20
<210>	53	
<211>	20	
<212>		
<213>	Artificial sequence	
<220>		
<223>	Synthetic oligonucleotide	
<400>	53	
		20
<210>	54	
<211>	20	
<212>	DNA	
<213>	Artificial sequence	
<220>		
<223>	Synthetic oligonucleotide	
<400>	54	
		20
<210>	55 .	
<211>	20	
<212>	DNA	
<213>	Artificial sequence	

<220>	Synthetic oligonucleotide	
~2237	Synthetic originatiootide	
<400>	55	
tccatga	acgt ctttgatgtt	20
<210>	56	
<211>	20	
<212>		
<213>	Artificial sequence	
<220>		
<223>	Synthetic oligonucleotide	
	•	
<400>	56	
tccatga	acgt atttgatgtt	20
<210>	57	
<211>		
<212>	DNA	
<213>	Artificial sequence	
<220>	Complete alignment active	
<223>	Synthetic oligonucleotide	
<400>	57	
tccatga	acgt gtttgatgtt	20
.010-	50	
<210> <211>		
<212>		
	Artificial sequence	
<220>		
<223>	Synthetic oligonucleotide	
<400>	58	
	tttt gtegttttgt egtt	24
<210>	·	
<211> <212>	DNA	
<213>	Artificial sequence	
<220>		
<223>	Synthetic oligonucleotide	
<400>	59	24
raceac	tttt gtgcttttgt gctt	24
<210>	60	
<211>	20	
-212-	אזאר	

```
<213> Artificial sequence
 <220>
 <223> Synthetic oligonucleotide
 <400> 60
 tccatgacgt tcctgatgct
                                                                      20
 <210> 61
 <211> 20
 <212> DNA
 <213> Artificial sequence
 <220>
 <223> Synthetic oligonucleotide
 <400> 61
 tccatgagct tcctgatgct
                                                                     20
 <210> 62
 <211> 16
 <212> PRT
 <213> Artificial sequence
 <220>
<223> Consensus oligopeptide
 <220>
<221> MISC_FEATURE
<222> (4)..(5)
<223> Any amino acid
<220>
<221> MISC_FEATURE
<222> (7)..(12)
<223> Any amino acid
<220>
<221> MISC_FEATURE
<222> (14)..(15)
<223> Any amino acid
<400> 62
Gly Asn Cys Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Xaa Xaa Cys
     5
<210> 63
<211> 16
<212> PRT
<213> Homo sapiens
<400> 63
```

- 111 -

```
Gly Asn Cys Arg Arg Cys Asp His Ala Pro Asn Pro Cys Met Glu Cys
<210> 64
<211> 16
<212> PRT
<213> Mus musculus
<400> 64
Gly Asn Cys Arg Arg Cys Asp His Ala Pro Asn Pro Cys Met Ile Cys
      5
<210> 65
<211> 31
<212> PRT
<213> Artificial sequence
<220>
<223> Consensus oligopeptide
<220>
<221> MISC_FEATURE
<222> (2)..(8)
<223> Any amino acid
<220>
<221> MISC_FEATURE
<222> (10)..(10)
<223> Any amino acid
<220>
<221> MISC_FEATURE
<222> (12)..(12)
<223> Any amino acid
<220>
<221> MISC_FEATURE
<222> (14)..(22)
<223> Any amino acid
<220>
<221> MISC_FEATURE
<222> (25)..(30)
<223> Any amino acid
<400> 65
Arg Xaa Xaa Xaa Xaa Xaa Xaa Arg Xaa Asp Xaa Tyr Xaa Xaa Xaa
            5
```

```
Xaa Xaa Xaa Xaa Xaa Arg Ser Xaa Xaa Xaa Xaa Xaa Tyr
                                      25
  <210> 66
  <211> 31
  <212> PRT
  <213> Homo sapiens
  <220>
 <221> MISC_FEATURE
<222> (2)..(8)
<223> Any amino acid
 <220>
 <221> MISC_FEATURE
 <222> (10)..(10)
 <223> Any amino acid
 <220>
 <221> MISC_FEATURE
<222> (12)..(12)
<223> Any amino acid
 <220>
 <221> MISC_FEATURE
 <222> (14)..(22)
 <223> Any amino acid
 <220>
<221> MISC_FEATURE
<222> (25)..(30)
<223> Any amino acid
<400> 66
Gln Xaa Xaa Xaa Xaa Xaa Xaa Lys Xaa Asp Xaa Tyr Xaa Xaa Xaa
Xaa Xaa Xaa Xaa Xaa Arg Leu Xaa Xaa Xaa Xaa Xaa Tyr
                                    25
<210> 67
<211> 31
<212> PRT
<213> Mus musculus
<220>
<221> MISC_FEATURE
<222> (2)..(8)
<223> Any amino acid
```

```
<220>
<221> MISC_FEATURE
<222> (10)..(10)
<223> Any amino acid
<220>
<221> MISC_FEATURE
<222> (12)..(12)
<223> Any amino acid
<220>
<221> MISC_FEATURE
<222> (14)..(22)
<223> Any amino acid
<220>
<221> MISC_FEATURE
<222> (25)..(30)
<223> Any amino acid
<400> 67
Gln Xaa Xaa Xaa Xaa Xaa Xaa Lys Xaa Asp Xaa Tyr Xaa Xaa Xaa
1 5
                                    10
Xaa Xaa Xaa Xaa Xaa Xaa Gln Leu Xaa Xaa Xaa Xaa Xaa Tyr
<210> 68
<211> 31
<212> PRT
<213> Homo sapiens
<400> 68
Gln Val Leu Asp Leu Ser Arg Asn Lys Leu Asp Leu Tyr His Glu His
Ser Phe Thr Glu Leu Pro Arg Leu Glu Ala Leu Asp Leu Ser Tyr
                   25
<210> 69
<211> 31
<212> PRT
<213> Mus musculus
<400> 69
Gln Val Leu Asp Leu Ser His Asn Lys Leu Asp Leu Tyr His Trp Lys
```

1 5 10 15

Ser Phe Ser Glu Leu Pro Gln Leu Gln Ala Leu Asp Leu Ser Tyr 20 25 30

<210> 70

<211> 20

<212> DNA

<213> Artificial sequence

<220>

<223> Synthetic oligonucleotide

<400> 70

tccaggactt ctctcaggtt

20

- 115 -